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Ambulatory Pain Management Guideline			
Pain Management Guideline Team			
Team leads			
Jill N. Fenske, MD, <i>Family Medicine</i>			
Daniel W. Berland, MD, <i>General Medicine / Anesthesiology</i>			
Team members			
SriKrishna Chandran, MD, <i>Physical Medicine & Rehabilitation</i>			
R. Van Harrison, PhD, <i>Learning Health Sciences</i>			
Jill Schneiderhan, MD, <i>Family Medicine</i>			
Paul E. Hilliard, MD, <i>Anesthesiology</i>			
Consultants			
Kimberly C. Bialik, PhD, <i>Anesthesiology</i>			
Daniel J. Clauw, MD, <i>Anesthesiology</i>			
Desmond A. Lowe, BS, <i>Medical Student</i>			
Kathleen S. Mehari, MD, <i>Obstetrics & Gynecology</i>			
Michael A. Smith, PharmD, <i>College of Pharmacy</i>			
Susan G. Urba, MD, <i>Hematology/Oncology</i>			
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Karl T. Rew, MD			

R. Van Harris, PhD

April L. Proudlock, RN

Patient Population. Adults with acute or chronic pain, including cancer patients, without progressive or terminal disease, treated in an outpatient setting, excluding hospice and end-of-life care.

Objectives. Provide a framework for comprehensive pain evaluation and individualized multimodal treatment. Improve quality of life and function in patients experiencing pain, while reducing the morbidity and mortality associated with pain treatments, particularly opioid analgesics.

Key Points

Acute Pain

Pain resolution. Acute pain is associated with tissue damage. As tissue heals, pain should resolve.

Limit opioid therapy. Avoid opioids for mild to moderate acute pain [IC]. Consider opioids for moderately-severe to severe acute or procedural pain [IIC], but if used, limit dose and duration. Do not prescribe opioids for sprains, lacerations, skin biopsies, or simple dental extractions [IIIE].

Chronic Pain

Chronic pain differs from acute pain. Chronic pain is not acute pain that failed to resolve. It is a distinct condition that is better understood as a disease process than as a symptom. Use a biopsychosocial approach in assessment and management.

Diagnosis

Chronic pain assessment. Perform a history and physical examination. Assess pain characteristics, pain treatment history, quality of life and functional impact, pain beliefs, and psychosocial factors. Assess comorbid conditions, including medical and psychiatric conditions, substance use, pain beliefs and expectations, and suicidality (Table 3) [IC]. Review any pertinent diagnostic studies [IC].

Mechanism. Classify chronic pain as primary or secondary. Determine the underlying neurobiologic mechanism of pain: nociceptive, neuropathic, central (nociplastic). Assign the diagnosis of an underlying chronic pain syndrome, when applicable. (Table 2) [IC].

Treatment

Create an individualized treatment plan (Table 4) utilizing multiple modalities, including non-pharmacologic (Tables 5-6) and non-opioid pharmacologic (Table 7) interventions [IC]. Use shared decision-making. Emphasize interventions with the lowest risk [IC].

Assess response, address barriers to implementation and adjust the treatment plan [IC].

Generally, avoid opioid therapy. Opioids are not indicated for most patients with chronic pain (Figure 1) [IB]. If considering starting or continuing an opioid, thoroughly assess the risk of harm before proceeding [IB], and perform a full evaluation, including record review, urine comprehensive drug screen, and review of the state prescription drug monitoring program report (MAPS in Michigan). Potential benefits of opioid use must clearly outweigh risks [IE].

Obtain informed consent when prescribing opioids. Use the Start Talking Form and Controlled Substance Agreement. Provide opioid education. Discuss benefits and harms [IE].

Opioid Management (Figure 2)

Regular visits/assess patients on chronic opioid therapy regularly, at least every 2-3 months (Table 9) [IE]. With each prescription, review benefits versus risks of therapy [IE]. Titrate (adjust) the dose to clinical effect and consider whether taper is indicated.

Monitor closely. Review the state prescription drug monitoring program (PDMP) report with each prescription [IE]. Calculate and monitor morphine milligram equivalents per day (MME/day) (Appendix C). Perform a urine drug screen at least once per year, and more often for patients who are at more than minimal risk [IE] (Appendix D). Watch for red flag behaviors (Table 10).

Indications for opioid discontinuation. If functional goals have not been met, adverse effects occur, or medication misuse is present (Table 10), consider opioid dose reduction, discontinuation, or conversion to buprenorphine [IIE]. In cases of opioid diversion, discontinue opioids [IE] and contact local law enforcement. In less urgent situations, discontinue using a rapid or slow taper [IE] (see Appendix F).

Screen for opioid use disorder. Assess for opioid use disorder, and consider complex persistent dependence [IE]. When present, refer to a specialist or offer treatment, including buprenorphine [IE].

* **Strength of recommendation:** I = generally perform; II = may be reasonable to perform; III = generally do not perform.

Level of evidence supporting a diagnostic method or an intervention: A = Systematic review of randomized controlled trials; B = randomized controlled trials; C = systematic review of nonrandomized controlled trials, nonrandomized controlled trials, group observation studies; D = Individual observation descriptive study; E = expert opinion.

Table 1. Acute Pain Overview by Severity and Cause

Level of Pain	Examples	Opioid Indicated	Therapeutic Options to Consider
Spontaneous / Traumatic			
Mild	Muscle ache after yardwork, tension headache, superficial abrasion/burn	No	NSAIDs, acetaminophen, rest, ice
Moderate	Simple bone fracture, sprain, deep laceration	No	Immobilization for fracture. NSAIDs, acetaminophen, rest, ice
Severe	Complex fracture, deep thermal injury, traumatic amputation	Yes	Consider alternatives to opioids, such as local interventions, based on type of pain expected. Consult Acute Pain Service.
Anticipated / Procedural			
Mild	Phlebotomy, skin biopsy, dental extraction	No	NSAIDs, acetaminophen, consider topical lidocaine
Moderate	Ambulatory surgery, complex dental extraction	Maybe – depends on extent of surgery. See	NSAIDs, acetaminophen, rest, ice, peripheral nerve block/catheter, topical local anesthetics

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Severe	Multilevel spinal fusion, large intra-abdominal surgery, Arthroplasty	Yes – develop weaning plan. Consider intranasal Naloxone	NSAIDs, acetaminophen, rest, ice, peripheral nerve block/catheter, topical local anesthetics, membrane stabilizers, epidural catheter

Table 2. Classification of Chronic Pain Syndromes and Relationship to Neurobiologic Mechanism of Pain

Pain Type	Definition	Neurobiologic Mechanism	Examples
Chronic Primary Pain			
1. Chronic widespread pain	Widespread pain persisting for longer than 3 months, associated with emotional distress or functional disability	Central sensitization	Fibromyalgia
1. Complex Regional Pain Syndrome	Disorder of body region, usually distal limbs, characterized by pain (allodynia), swelling, loss of function, vasomotor instability, skin changes	Neuropathic Central sensitization	Chronic Regional Pain Syndrome (formerly reflex sympathetic dystrophy)
1. Chronic primary headache/ orofacial pain	Idiopathic headache or orofacial pain, not secondary to another condition	Nociceptive Neuropathic Central sensitization	Chronic migraine or temporomandibular disorder
1. Chronic primary visceral pain	Persistent or recurrent pain originating from internal organs, without a clear organic cause	Central sensitization	Irritable bowel syndrome
1. Chronic primary musculoskeletal pain	Chronic pain experienced in muscles, bones, joints, or tendons that cannot be attributed directly to a known disease or tissue damage process ²	Nociceptive Neuropathic Central sensitization	Non-specific low back pain
Chronic Secondary Pain			
1. Chronic cancer-related pain	Pain caused by the cancer itself (by the primary tumor or by metastases) or by its treatment (surgery, chemotherapy, or radiotherapy) ³	Nociceptive Neuropathic Central sensitization	Chronic cancer pain, chronic cancer treatment pain (eg, chemotherapy-induced peripheral neuropathy, radiation fibrosis)

1. Chronic postsurgical or posttraumatic pain	Pain secondary to surgery or trauma which persists for longer than 3 months	Nociceptive Neuropathic Central sensitization	Incisional pain, nerve injury due to trauma or surgery (eg, persistent whiplash or low back pain after trauma)
1. Chronic neuropathic pain	Pain caused by a lesion or disease of the somatosensory nervous system ⁵	Neuropathic	Trigeminal neuralgia, chronic painful polyneuropathy (eg, diabetic polyneuropathy), postherpetic neuralgia
1. Chronic secondary headache/ orofacial pain	Headaches or orofacial pains, secondary to a medical condition	Nociceptive Neuropathic Central sensitization	Head/face pain secondary to trauma, tumor, hemorrhage, etc.
1. Chronic secondary visceral pain	Persistent or recurrent pain originating from internal organs, due to a secondary cause	Nociceptive	Abdominal pain due to adhesions or ischemia
1. Chronic secondary musculoskeletal pain	Persistent or recurrent pain that arises as part of a disease process directly affecting bones, joints, muscles, or related soft tissues	Nociceptive	Rheumatoid arthritis, osteoarthritis

Note: Adapted from Treede, RD, Rief w, Barke A, et.al, Chronic pain as a symptom or disease: the IASP classification of chronic pain for the International Classification of Diseases (ICD-11. Pain, Jan 2019, 160 (1):19-27¹

Table 3. Initial Evaluation of Chronic Pain

Subjective Assessments

History of present illness for pain concern:

Onset: When did pain start? Was there an inciting event?

Time Course: How has the pain changed over time? Is it constant or intermittent?

Location: Utilize a body map drawing (Appendix A1).

Quality: Aching, throbbing, tight (musculoskeletal). Shooting, burning or electric pain (neuropathic).

Poorly localized, deep, gnawing pain (visceral).

Intensity and Function: Pain intensity scales are of limited utility for chronic pain. Focus on the functional assessment. Consider using the PEG scale (Appendix A2).

Provocative Factors: Relevant positions, functions, or activities that increase pain.

Palliative Factors: Relevant positions, functions, or activities that decrease pain.

Associated Factors: Signs and symptoms associated with pain, including somatic symptoms: fatigue, trouble thinking or remembering, or waking up unrefreshed.

Pain treatment history: Non-pharmacologic treatments (eg, physical therapy, transcutaneous electrical stimulation [TENS], acupuncture, chiropractic), OTC medications, prescribed medications, and invasive diagnostic or therapeutic procedures (eg, nerve blocks, stimulation trials, epidural injections, surgery).

How did these interventions impact pain or change it?

Past medical history, past surgical history

Chronic health conditions: Cardiopulmonary disease, obstructive sleep apnea, renal disease, liver disease.

Reproductive health status: Pregnancy, contraception.

Psychiatric history: Depression, anxiety/panic, substance use disorder, hallucinations, PTSD, complex PTSD, personality disorders, suicide attempt, hospitalization, treatment history.

Suicide risk assessment. [Columbia Suicide Severity Rating Scale \(C-SSRS\)](#)

Surgery related to pain concerns.

Medications/Allergies

Current medications and supplements: effectiveness, adverse effects.

Previous medication trials: NSAIDs, SSRIs, SNRIs, tricyclic antidepressants (TCAs), anticonvulsants, opioids, gabapentinoids, syndrome specific drugs (eg, triptans), topical trials, acetaminophen.

Allergies and intolerances.

Family history: Chronic pain, substance use disorders, psychiatric disorders.

Social history:

Living arrangement, interpersonal relationships

Level of education

Work history/status

Insurance status

Legal matters (eg, disability, lawsuits, criminal charges)

Lifestyle (sleep, exercise, diet)

Substance use (Alcohol, tobacco, marijuana, illicit drugs, caffeine)

History of trauma, adverse childhood experiences

Social stressors, support, food or housing insecurities, access to resources, spirituality

Pain beliefs and response to pain

Review of systems: 14 system questionnaire. Cognitive screen, such as [Montreal Cognitive Assessment](#).

Objective Assessments

Physical exam

Imaging, EMG, lab tests

Urine comprehensive drug testing (EIA + GC/MS, or LC/MS-Controlled Med Management Panel at UM)

Check PDMP (MAPS in Michigan). Look for multiple prescribers, use of multiple pharmacies, unreported controlled substances, or other red flag behaviors (Table 10).

Table 4. Creating an Individualized Pain Treatment Plan

Overarching principles:

Use shared decision making

Emphasize interventions with the lowest risks.

Make non-pharmacologic interventions a necessary component of all plans.

Avoid opioid therapy for most patients (Figure 2).

1. Initial assessment

Determine neurobiological pain type, underlying mechanism(s) of pain (nociceptive, neuropathic,

central)
Determine comorbidities and psychosocial factors

2. Establish a therapeutic alliance

Set goals for improved function. Goal is to function despite pain - patients miss this distinction.
Use SMART acronym (Specific goal, Measurable; Attainable; Relevant and Time-based)
Provide pain psychoeducation and facilitate self-management.

3. Initiate non-pharmacologic interventions

Tier 1: Lifestyle changes
Tier 2: Targeted therapies (Table 5)

4. Consider additional interventions

Non-opioid pharmacologic therapy (Table 7).
Procedural interventions (eg, epidural or joint injection, trigger point injection, surgery)

5. Monitor

Assess response.
Address barriers to implementing treatment plan.
Adjust treatment plan as needed (repeat steps 2-5).
If lack of response to multimodal pain treatment plan, consider referral.

Table 5. Non-pharmacological Pain Treatment Options

Non-Pharmacological Options	Nociceptive	Neuropathic	Central Sensitization
Consider in all patients			
Increased Activity/ Exercise (aerobic, strength, flexibility/ balance)	In addition to helping generally across types of pain, specifically:		
	Knee and hip osteoarthritis Rheumatoid arthritis Vascular claudication,	Chemotherapy induced neuropathy Diabetic peripheral neuropathy Multiple sclerosis	Fibromyalgia (for pain, aerobic exercise rather than resistance exercise)
Improve Sleep	All types of pain		
Dietary Modification	For all types of pain: Mediterranean pattern of eating		
Self-regulatory and psychophysiological approaches	For all types of pain: biofeedback, relaxation training, and hypnosis		
Consider in select patients based on diagnosis and interest			
Acupuncture	Osteoarthritis, chronic neck and	Post-herpetic neuralgia, chemotherapy induced	Fibromyalgia

	low back pain, Headache	polyneuropathy	
Physical Therapy	Functional deficits or secondary pain generators that directed therapy may improve (based on functional deficits rather than diagnosis)		
Transcutaneous electrical stimulation (TENS)	Rheumatoid arthritis Knee osteoarthritis	Diabetic peripheral neuropathy Post herpetic neuralgia	Fibromyalgia
Massage	Low back pain Knee osteoarthritis Neck pain Hand osteoarthritis		Fibromyalgia
Mindfulness Based Stress Reduction	Low back pain Rheumatoid arthritis		Fibromyalgia
Cognitive behavioral therapy (CBT)	Low back pain Neck pain Knee pain Shoulder pain Hip pain, Hip osteoarthritis Knee osteoarthritis Rheumatoid arthritis Systemic lupus erythematosus Temporomandibular joint pain.		Fibromyalgia
Acceptance and commitment therapy (ACT)	Low back pain Rheumatoid arthritis		Fibromyalgia

Table 6. Herbal Supplements Used in Chronic Pain*

Name	Proposed Indication	Proposed Effect	Side Effects/Notes
<i>Arnica montana</i> (topical) ²	Low back pain – acute flares Muscle pain Osteoarthritis	Anti-inflammatory	Oral use may be toxic
<i>Boswellia serrata</i> ³	Osteoarthritis	Anti-inflammatory	
Cannabinoids ⁴	Neuropathic pain Osteoarthritis	CBD: Anti-inflammatory THC:	Quality of evidence is low to date with only real benefit a mild one in pain reduction for neuropathic pain.

	Headache	Central nervous system mediated	CBD may play an anti-inflammatory role, with THC causing most adverse effects. Consider advising patients who are planning to use for pain management to start with low dose CBD alone.
Cayenne (topical) ²	Low back pain –acute flares	Analgesic Anti-Inflammatory	Equal to placebo
Devil's claw 60-100 mg(standardized hapagosides) / day in divided dosing (Harpagophytum) ²	Low back pain – acute flares	Analgesic Anti-inflammatory	No evidence for use in other pain conditions
Glucosamine and chondroitin ⁵	Osteoarthritis		May interact with warfarin. Does not treat pain from knee or hip OA. Does not slow the progression of knee or hip OA. Does not have disease modifying effects in knee or hip OA.
Turmeric ⁶	Osteoarthritis	Anti-inflammatory	Case reports of antiplatelet effect but only clinical trial showed no impact on bleeding or INR.
Willow bark 120 to 240 mg/day ²	Low back pain – acute flares	Analgesic Anti-inflammatory	Contains salicin, an aspirin precursor. Avoid if allergic to ASA or NSAIDs.

- Always check for potential interactions of herbal supplements with prescription medications or other non-prescription medications or supplements.

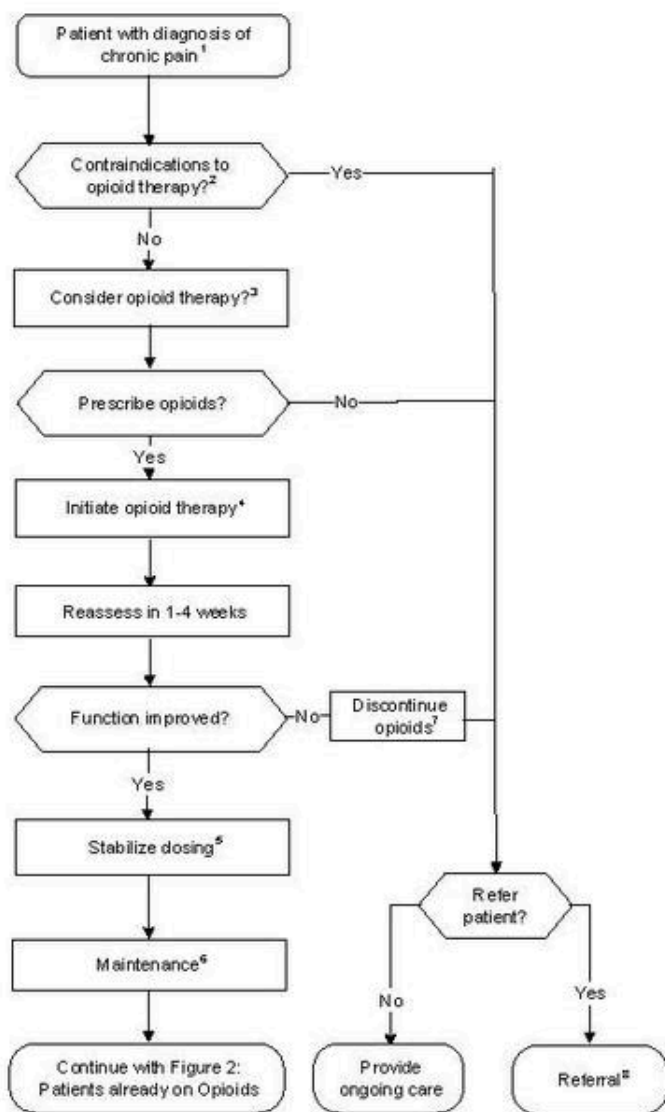
Table 7. Non-Opioid Medications for Pain

Medication	May Benefit	Potential Co-treatment Of	Harms	Cost	Comments
Acetaminophen	Nociceptive	Headaches	May exacerbate chronic daily headaches	Low	May be synergistic when combined with NSAIDs
NSAIDs	Nociceptive	Headaches	Gastrointestinal bleeding, acute kidney injury, chronic kidney disease, increased risk for coronary	Low	May increase blood pressure; edema. COX-2 inhibitor somewhat decreases risk of gastrointestinal

			artery events		bleeding
SNRIs Duloxetine, venlafaxine, milnacipran	Central pain sensitization (Type 1) pains, neuropathic pain, non-specific low back pain, functional abdominal pain	Anxiety Depression	Weight gain, urinary retention, withdrawal symptoms (taper down to discontinue)	Low/ Moderate	Duloxetine FDA-approved for diabetic neuropathy, fibromyalgia Duloxetine more effective than venlafaxine
Anticonvulsants Gabapentin Pregabalin Topiramate	Neuropathic pain, fibromyalgia Neuropathic pain	Gabapentin: menopausal hot flushes Migraine prophylaxis	Weight gain, edema, fatigue Cognition and speech problems	Gabapentin: Low Pregabalin: Low Topiramate: Moderate	Gabapentin: not effective in low back pain Pregabalin: FDA-approved for diabetic neuropathy, fibromyalgia
Tricyclics	Central, neuropathic	Anxiety, depression, insomnia, migraine prophylaxis, smoking cessation	Fatigue, weight gain, constipation	Low	Give in early evening when sleep initiation is an issue
Muscle relaxants Cyclobenzaprine, methocarbamol, tizanidine, Benzodiazepines (BZD), carisoprodol – <i>see comments</i> Baclofen	Muscle spasms Spasticity		Fatigue Sedation, dependence Same as benzodiazepines	Low/High	Not effective for acute or chronic back pain. <i>Benzodiazepines, carisoprodol (Soma): neither indicated nor effective – high risk for dependence</i> Same as benzodiazepines
Topical Agents NSAIDs Lidocaine ointment or patch Capsaicin cream Nitroglycerin	Osteoarthritic (OA) joints OA joints, focal neuropathic pain Same as lidocaine Wound, anal fissure pain, vulvodynia, diabetic		Headaches	High/Very High High/Very High Low Low	Ointment is messy. Patches often not covered by insurance Do not use nitroglycerin in patients using PDE-5 erectile dysfunction medications

	neuropathy					
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Figure 1. Prescribing Opioids for Chronic Pain in Opioid Naïve Patients (Not Including Active Cancer)



¹ Diagnosis of Chronic Pain

Perform evaluation (Table 3).
Determine underlying mechanisms of pain, primary and secondary causes.
Try non-pharmacological treatments (Table 5).
Try non-opioid pharmacological treatments/herbal (Tables 6, 7).

² Contraindications

Benzodiazepines/sedatives
Comorbidities (Table 8).
Red flag behaviors (Table 10).
Evidence of central pain

³ Consider Opioid therapy

Discuss goals of therapy, functional improvement, expectations (pain-free may not be possible), risks, exit strategy (reduce dose, taper dose, discontinue).

⁴ Initiate Opioid Therapy

Check prescription drug monitoring database.
Discuss goals of therapy, functional improvement, expectations (pain-free may not be possible), risks, exit strategy (reduce dose, taper down, discontinue).
Educate and document: Start Talking Form and Controlled Substance Agreement.
Initiate short-acting, low dose < 20 MME/day.

⁵ Stabilize Dose

Evaluate for opioid induced hyperalgesia.
Titrate dosing over 2-4 weeks.
Consider converting short-acting to long-acting formulations.
Naloxone rescue strategy.

⁶ Maintenance

In-person visits every 3 months.
Reevaluate: response to treatment, non-pharmacologic therapies.
Consider: reducing or tapering down dose of opioid; transitioning to buprenorphine or non-opioids; need for naloxone.
Check prescription monitoring database prior to every refill; periodic pill counts
Urine drug screen annually.

⁷ Discontinue

Goal of therapy not met.
Adverse effects outweigh benefit.
Concern for addiction or diversion.
Medical condition deteriorates.

⁸ Refer Patient

Integrative Medicine
Interventional Pain Management
Medical Pain Management/Addiction Specialist
Physical Medicine and Rehabilitation
Pain Psychology
Physical Therapy
Rheumatology

Figure 2. Prescribing Opioids for Chronic Pain

in Patients Already on Opioids (Not Including Active Cancer)

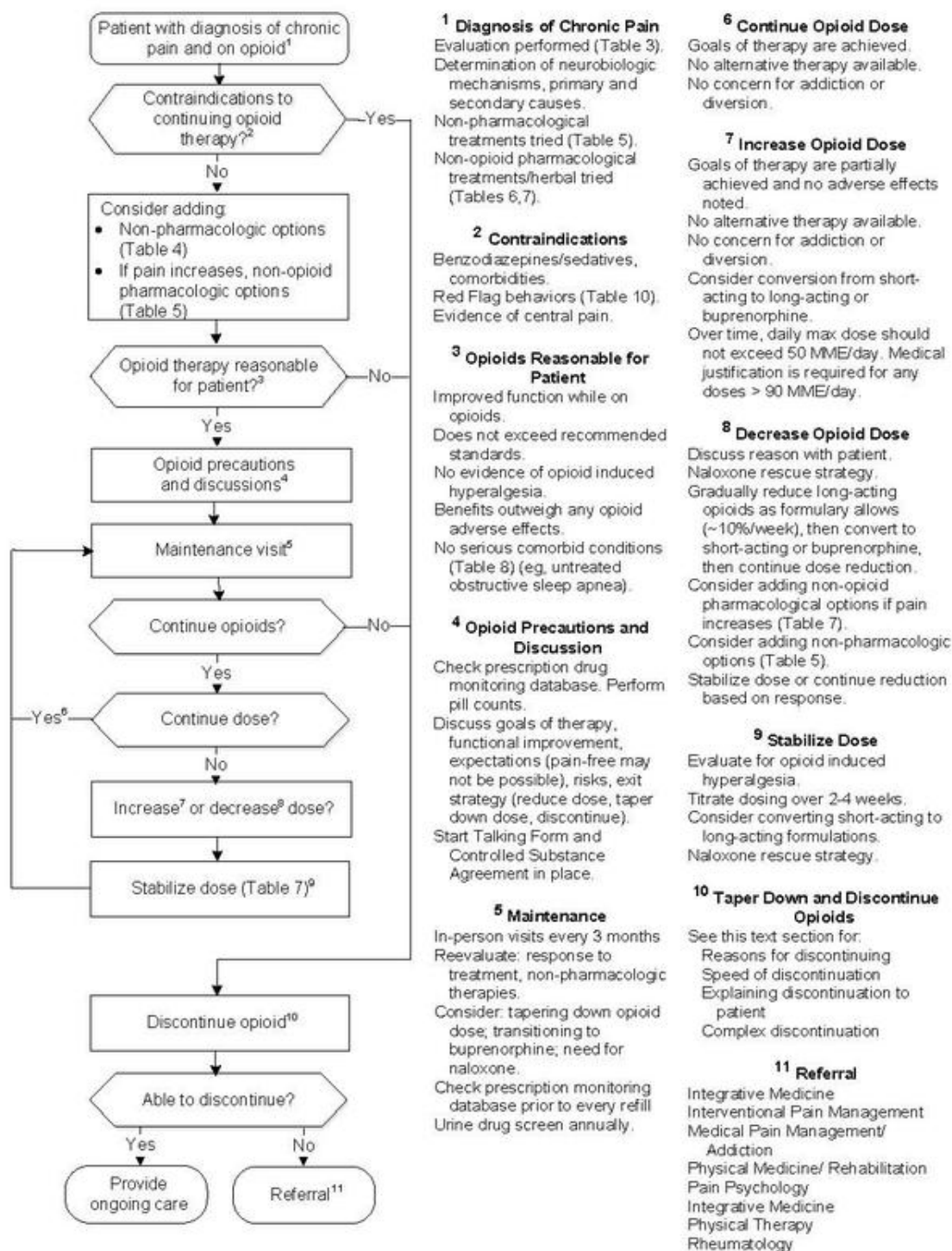


Table 8. Special Populations for Whom Opioids

Increase Risks

Risks of opioid therapy are higher in these populations. Non-pharmacologic and non-opioid pharmacologic therapies are preferred.

Population	Considerations and Actions
Women of Reproductive Age, Pregnancy, and Breast-feeding	<p>Women who may become pregnant: Offer pregnancy testing and provide contraceptive counseling prior to initiating opioids.⁷</p> <p>Pregnant women: Provide counseling on the risk of opioids in pregnancy, including risks to the fetus, prior to initiating opioids.⁷</p> <p>Breast-feeding women: Do not prescribe codeine or tramadol.⁸</p>
Pediatrics	<p>Do NOT prescribe codeine or tramadol in patients under age 12 and avoid use in most patients under age 18.⁸</p> <p>Obtain informed consent from a parent or guardian prior to initiating opioids in patients under age 18. Advise the parent or guardian to supervise the use of the opioid prescription.^{7,9}</p>
Geriatrics	<p>Assess fall risk, cognition, respiratory status, and renal function prior to prescribing opioids.⁷</p> <p>Reduce the initial dose of opioids by 25-50% for patients older than 60; titrate the dose slowly.¹⁰</p>
Sleep-Disordered Breathing	<p>Do NOT prescribe opioids to patients with moderate or severe sleep-disordered breathing whenever possible.¹¹</p> <p>Carefully titrate and monitor opioid doses for patients with mild sleep-disordered breathing.¹¹</p>
Cardiopulmonary Disorders	<p>Carefully titrate and monitor opioid doses for patients with cardiopulmonary disorders, as these conditions may predispose patients to hypoxemia or sleep-disordered breathing, which could be compounded by opioid use.</p>
Renal Disease	<p>Renally-adjust opioid doses and titrate slowly for patients with chronic kidney disease. Medications may require a reduction in dose frequency, with increased intervals between doses.¹²</p> <p>Avoid morphine, codeine, tapentadol, and extended release tramadol in patients with CKD due to decreased renal clearance. Reduce the dose of hydrocodone, if prescribed.</p> <p>Consider prescribing tramadol (maximum frequency BID) or oxycodone for moderate pain. Consider hydromorphone, methadone or fentanyl for severe pain. Buprenorphine may also be used.</p>

Liver Disease	<p>Reduce opioid doses and titrate slowly for patients with advanced liver disease or cirrhosis.¹³</p> <p>Avoid codeine in patients with hepatic dysfunction due to impaired drug metabolism.</p> <p>Use hydrocodone, tramadol, and buprenorphine with caution due to potentially impaired drug metabolism in patients with cirrhosis.</p> <p>Consider prescribing oxycodone, hydromorphone, methadone or fentanyl, which have a more favorable safety profile for patients with liver disease.</p>
Neurologic Disorders	<p>Avoid or minimize use of opioids in patients with chronic debilitating neurologic disorders, including CVA, movement disorders, neurodegenerative disorders, and dementia.</p> <p>Assess fall risk, cognition, respiratory status, and risk for sleep disordered breathing prior to prescribing opioids.</p> <p>Reduce the initial dose of opioids by 25-50% and titrate slowly.</p>

Table 9. Visit Checklist for Patients on Chronic Opioids

Determine level of adherence to both pain and general medical management plans (medications, physical therapy, lifestyle interventions, etc.). Identify and address barriers to adherence.

Document progress toward functional goals and pain response.

Evaluate for adverse effects of medications (NSAIDs, opioids, or other medications).

Evaluate status of medical or psychiatric comorbidities.

Update social history (change in psychosocial determinants, substance use).

Assess for red flag behaviors that may indicate addiction or diversion (Table 10). Review written pain management agreement for patients at risk.

Check PDMP (MAPS in Michigan) with each prescription. Watch for multiple prescribers, use of multiple pharmacies, unreported controlled substances. Pill counts for high risk patients

Order a urine drug screen at least once per year (more frequently if red flag behaviors are present).

Assure that a Controlled Substance Agreement has been reviewed with patient and scanned to the record.

Prescribe naloxone if opioid dosage is > 50 MME/day, or if there is a history of overdose, concurrent benzodiazepine use, or comorbidities that increase the risk for overdose.

Revise Individualized Pain Treatment Plan as needed:

- Titrate effective medications, and stop ineffective medications (including NSAIDs, gabapentin and opioids).
- Consider new modalities and incorporate non-pharmacologic treatments (Table 4).
- Taper down the opioid dose when there is no improvement in function, or when there is risk for harm or opioid use disorder. Consider buprenorphine.

Evaluate for appropriate boundaries in the therapeutic relationship.

Consult appropriate specialist(s) if there is evidence of opioid use disorder, failure to reach functional goals despite adherence to plan, a need for rapidly escalating or very high dose opioids, active

psychiatric comorbidities, or negative affect or pain beliefs.
Consider need for naloxone.

Table 10. Red Flag Behaviors That May Indicate Addiction or Diversion¹⁴

Threatening/aggressive behavior toward staff or prescriber	Fixating on controlled substances or requests for drugs by name
Sedated/intoxicated appearance	Requests for early refills of controlled substances
Refusal to authorize release of medical records	Lost or stolen controlled substance prescriptions
Refusal to sign Controlled Substance Agreement	Prescription tampering or forgery
Refusal to try non-opioid therapies not previously prescribed	Misuse of controlled substances (obtaining from family, friends, or on the street)
Concurrent use of multiple pharmacies	History of suspicion of controlled substance diversion
Recurrent emergency department pain visits for non-emergent pain	Continuing to request and take opioids despite a lack of benefit and/or in the face of toxicity
Obtaining controlled substances from multiple prescribers	
Allergies or intolerances to multiple non-opioid analgesics	

Clinical Problem and Current Dilemma

Pain is often undertreated or incorrectly treated.
Chronic pain affects 50-80 million Americans.
Primary care clinicians manage the majority of patients with chronic pain.
The nationwide opioid epidemic adds complexity to the management of chronic pain.

Pain is the most common reason for which individuals seek health care. Effective pain management is a core responsibility of all clinicians, and is a growing priority among clinicians, patients, and regulators. Despite increased attention, many patients' pain remains under-treated or incorrectly treated.

The prevalence of chronic pain in the US is difficult to estimate, but its impact is profound. Fifty to eighty million Americans experience daily pain symptoms. The cost of pain management is approximately \$90 billion annually. Chronic pain is the leading cause of long-term disability in the US. These numbers will only increase as our population ages, amplifying the need for effective, accessible interventions to manage chronic pain and preserve function.

While multidisciplinary subspecialty pain services are increasingly available, primary care clinicians will continue to manage the majority of patients with chronic pain. This care can be challenging and resource-intensive, and many clinicians are reluctant or ill-equipped to provide it.

The current nation-wide opioid epidemic adds another layer of complexity in the management of chronic pain. Opioids carry substantial risk for harm, and are not recommended for the majority of patients with chronic pain. However, due to high rates of opioid prescribing over the last 20-30 years, there are still many patients who remain on chronic opioid therapy. With the widespread adoption of the CDC opioid-prescribing guidelines in 2016¹¹, rates of opioid prescriptions have decreased. In some cases, inflexible application of these guidelines has led to patient abandonment and poor outcomes. Prescribers need training, resources, and support to manage patients taking opioid medications in a compassionate and safe manner. There is also a need for

better patient access to non-opioid pain management services and treatment for opioid use disorder.

This guideline is intended to support clinicians in evaluating and managing patients with pain and in navigating the complex issues involved with the use of opioids for pain management.

Acute and Subacute Pain – Overview

Definitions

Acute pain is associated with tissue damage and inflammation, with pain resolving as tissue heals.
Subacute pain, a subset of acute pain, may be present for 6 weeks to 3 months as tissue heals.
Chronic pain is a different medical condition involving abnormal peripheral or central neural function.

Acute pain is always associated with tissue damage; as tissue heals, pain should resolve. The definition of acute pain in the Michigan health code focuses on the cause and limited duration: "pain that is the normal, predicted physiological response to a noxious chemical, or a thermal or mechanical stimulus, and is typically associated with invasive procedures, trauma, and disease and usually lasts for a limited amount of time." The International Association for the Study of Pain (IASP) further emphasizes the time limit for acute pain: it is pain lasting less than 3 months.

Subacute pain is a subset of acute pain: pain that has been present for at least 6 weeks but less than 3 months. This definition reflects the process of tissue healing. The worst of the acute pain phase and inflammation is no longer present, but ongoing tissue healing is required for full resolution.

Chronic pain has little in common with acute pain and should be considered as a separate medical condition. Some differences are:

Acute Pain	Chronic Pain
Is a symptom	Is a diagnosis
Is associated with tissue damage	May or may not be associated with tissue damage
Lasts a limited time	Does not resolve quickly
May respond to opioid therapy for a limited time	Opioid therapy is generally not indicated
Has an inflammatory component	May or may not involve inflammation

The differing pathophysiology for acute pain and chronic pain requires different approaches to their diagnosis and treatment. Effective acute pain management has been shown to improve both patient satisfaction and treatment outcomes, and reduce the risk of developing chronic pain.

Diagnosis and Treatment

Recommendations:

Diagnose the cause of acute pain.

- Identify the medical or surgical condition for which acute pain is a symptom.
- Determine whether underlying cause is acute nociceptive pain or acute neuropathic pain.
- Assess the degree of functional impairment to help determine the urgency for addressing the acute pain issue.

Treating acute pain

- Consider the degree of tissue trauma, the patient's situation, and unique patient factors.
- Select a treatment appropriate for the underlying source of pain (nociceptive or neuropathic).
- Adjust the treatment plan if reinjury or pain exacerbation occurs during the subacute phase.

Diagnosis. Identify the medical or surgical condition for which acute pain is a symptom (see Table 1). Often the cause is obvious or revealed by the history. If the diagnosis is not immediately clear, history, physical examination, laboratory tests, and imaging may all be employed to arrive at the diagnosis.

Determine whether this is acute nociceptive pain (signaled to the brain via normally functioning afferent neural pathways) or acute neuropathic pain (dysfunctional neural functioning). Nociceptive and neuropathic pain are described in more detail below, under "General Approach to Chronic Pain". This classification helps guide the treatment plan and medications to prescribe.

In some cases, the cause is not immediately obvious, but the category of pain is. For example, burning pain starting in the neck and radiating into the fingers could be associated with acute cervical radiculopathy or may evolve to reveal zoster. Both are types of acute neuropathic pain. Strategies would include reducing inflammation, quieting of nerves, and further diagnostic work up to determine the exact cause. Weakness may point towards radiculopathy, while the presence of a rash points towards zoster.

Assess the degree of functional impairment to help determine the urgency for addressing the acute pain issue. For example, weakness may require a more aggressive strategy with early intervention, such as advanced imaging. If a patient is no longer able to carry on a usual routine or activities of daily living due to acute pain, an aggressive diagnostic workup is needed. An aggressive workup is also required in patients with a history of malignancy or immunosuppression.

Treatment. In the treatment plan, address both the underlying cause and the associated acute pain. In developing a treatment plan for the acute pain, consider the degree of tissue trauma, the patient's situation, and any unique patient factors. A patient in the immediate postoperative period after a major surgery will likely have more complex needs than a patient presenting for an ambulatory encounter.

The hallmark of acute pain is tissue inflammation. Acute pain can be nociceptive or neuropathic. Accordingly, measures to reduce inflammation are helpful when developing a treatment plan for acute pain conditions. Some treatments to consider for acute pain include those listed in the table below:

Nociceptive	Neuropathic
NSAIDs	Gabapentinoid anticonvulsants (gabapentin, pregabalin)
Acetaminophen	Topical anesthetics
Steroids	Duloxetine
	Nortriptyline/amitriptyline
Nerve blocks	Nerve blocks
Ice, rest, elevation	Capsaicin
Distraction, TENS unit	TENS unit
Physical therapy, stretching	Desensitization therapy
Opioid based medications	
Muscle relaxants <ul style="list-style-type: none"> • Oral magnesium • Methocarbamol 	

Plan for treatment of reinjury or exacerbation during the subacute pain phase. Often subacute pain occurs with increase in activity before tissue is completely restored to health. Have a plan to escalate analgesic needs for this well-defined occurrence. For example, anticipate how pain with physical therapy should be treated.

General Approach to Chronic Pain

Chronic pain is best understood as a disease process rather than a symptom.

Use a biopsychosocial approach when assessing and managing chronic pain.

Underlying mechanisms for chronic pain are:

- Nociceptive – tissue damage
- Neuropathic – sensory nervous system damage
- Central – heightened pain sensitivity in the central nervous system

Chronic pain has significant cognitive, affective, and interpersonal components.

Effective chronic pain management is focused on maximizing function and limiting disability, not just on reducing pain.

A chronic **primary** pain syndrome represents a disease that cannot be accounted for by another pain condition.

A chronic **secondary** pain syndrome initially manifests as a symptom of another disease and then continues after successful treatment of the disease.¹⁵

Biological and Psychosocial Factors

Chronic pain – pain that lasts or recurs for longer than 3 months – is not merely acute pain that does not resolve. Increasingly, chronic pain is recognized as a disease entity in and of itself, rather than as a symptom of another disease. Historically, pain has been viewed in a biomedical model, with a focus on identifying a specific pathologic cause of pain which can be treated through pharmacologic or interventional means. However, chronic pain is better understood by applying a biopsychosocial model. Chronic pain is a complex multi-dimensional condition, driven by the interplay of neurobiologic processes with psychosocial factors that may increase vulnerability or resilience to disease.¹⁶ A biopsychosocial approach allows the focus to move from the source of the pain to the management of its impact.

Neural mechanisms of Pain. Understanding the basic neurobiological mechanisms in chronic pain pathophysiology is important, since treatment approaches vary depending on these factors. There are three main subtypes of pain pathophysiology: nociceptive, neuropathic, and central sensitization. They are summarized below, with more detail regarding classification in Table 2.

Nociceptive pain is caused by tissue damage due to injury or inflammation, rather than harm to the central or peripheral nervous system. This is the primary type of pain involved in patients with arthritis, musculoskeletal inflammatory disorders (tendinitis, bursitis), or structural spine pain.

Neuropathic pain results from damage to the sensory nervous system. Patients typically describe electric, burning, or tingling sensations. Examples of neuropathic pain include post-herpetic neuralgia, diabetic neuropathy, and trigeminal neuralgia.

Central sensitization occurs when there is heightened pain sensitivity in the central nervous system that is not due to a peripheral pain signal generated by an injury or disease state. Central pain is driven by molecular and structural changes that occur in the central nervous system. It is the primary mechanism in conditions such as fibromyalgia, phantom limb syndrome, and chronic pelvic pain.

Psychosocial factors. Chronic pain has significant cognitive, affective and interpersonal components. Patients with chronic pain are more likely to report depression, anxiety, poor quality of life, and financial stress. They are five times more likely to use health care resources than patients without chronic pain. Pain beliefs and the individual and family response to chronic pain are also important factors.

Chronic Primary and Secondary Pain Syndromes

A classification system for chronic pain syndromes has been devised by the International Association for the Study of Pain (IASP), as outlined in Table 2.

Chronic primary pain syndromes. These syndromes represent a disease itself. A chronic primary pain syndrome is defined as pain in one or more anatomical regions that persists or recurs for longer than 3 months and is associated with significant emotional distress or functional disability (interference with activities of daily life and participation in social roles) and that cannot be better accounted for by another chronic pain condition.¹⁷

Chronic primary pain syndromes include:

- Fibromyalgia
- Complex regional pain syndrome
- Chronic primary headache and orofacial pain
- Chronic primary visceral pain
- Chronic primary musculoskeletal pain

Chronic secondary pain syndromes

Each of these syndromes initially manifests as a symptom of another disease. After healing or successful treatment, chronic pain may sometimes continue and hence the chronic secondary pain diagnoses may remain and continue to guide treatment (Table 2).¹⁵

Chronic secondary pain syndromes include:

- Cancer-related pain (eg, from tumor mass or treatment)
- Chronic postsurgical or posttraumatic pain
- Chronic neuropathic pain
- Chronic secondary headache or orofacial pain
- Chronic secondary visceral pain
- Chronic secondary musculoskeletal pain

Establishing the diagnosis of a specific chronic pain syndrome can be an important first step in providing clarity for the care team, psychoeducation for patients, and direction for treatment considerations. In order to arrive at a diagnosis, perform a thorough biopsychosocial assessment.

Biopsychosocial Assessment of Chronic Pain

Recommendations:

In addition to a usual history and physical examination, in patients with chronic pain assess the following (Table 3):

- Pain characteristics: location, quality, intensity and time course
- Pain treatment history
- Quality of life and functional impact

- Comorbid conditions, including medical comorbidities, psychiatric comorbidities, substance use disorders, and suicidality
- Pain beliefs and responses to pain
- Psychosocial factors
- Findings from physical exam and any pertinent diagnostic testing.

After reviewing the above, assign a diagnosis of chronic pain that identifies:

- The most likely neurobiologic etiologies of the pain: nociceptive, neuropathic, or central (Table 2)
- Whether it is a primary or secondary chronic pain syndrome.

Since chronic pain is a disease entity rather than a symptom of an underlying disease, a new strategy is needed to assess patients with chronic pain. Assessment should result in the diagnosis of a chronic pain syndrome and determine the underlying neurobiologic mechanism to help direct specific treatment strategies. Psychosocial assessment can help guide treatments in other domains regardless of the neurobiologic etiology.

The focus in chronic pain assessment differs from the evaluation of acute pain, which assumes a specific underlying injury or disease that treatment will cure. Begin chronic pain assessment with the history and physical examination. Important components of the initial evaluation are summarized in Table 3 and are detailed below. Assess pain characteristics, function, quality of life, comorbidities, pain beliefs, and social determinants. The physical examination may confirm a previous finding, exclude a serious or treatable abnormality, or diagnose an acute condition secondary to the chronic condition.

Pain Characteristics

Determine the location, quality, intensity, and time course of the pain. Pain intensity scales have a limited role in chronic pain.

Pain location. Pain drawings are frequently used for patients to identify the location of pain. A drawing on an anatomical outline can provide a quick impression of the breadth and character of the presenting pain complaint. However, quantitative ratings of pain drawings are not consistently associated with other aspects of pain disability. Therefore, pain drawings are not adequate to form clinical conclusions (eg, contribution of psychological causation for pain and disability).

Pain quality. A detailed account of pain quality may help identify potential types/sources of pain. Musculoskeletal or myofascial pain is often described as aching, throbbing or tight. Primarily neuropathic pain can be described as shooting, burning, or electric. Visceral pain may be gnawing, deep, and difficult to localize. Many patients will report more than one type of pain, but pain quality assessment will help guide treatment.

Pain intensity. A patient's report of pain intensity provides a subjective gauge of the distraction and interference pain causes in their daily life.

While pain intensity scales are useful in assessing and treating acute pain, they have a limited role in assessing and treating chronic pain. While chronic pain intensity is important to assess, ten-point pain scales that assess only pain severity or intensity (including various single-item written or visual scales) do not adequately assess broader functional effects of chronic pain. See below for pain scales that address the functional impact of pain and level of acceptance of pain.

Complete analgesia, which means achieving a pain assessment score of zero, is not possible for most patients with chronic pain. Use the intensity score in conjunction with the functional assessment to set treatment goals

and monitor treatment effectiveness. Analgesia without improved function is not a legitimate treatment goal.

Patients should understand that reducing pain intensity will not be the sole focus of evaluation or management. This requires a shift in expectations for many patients accustomed to an acute pain management model.

Pain time course. Evaluate changes in pain location, quality, and severity through time. Reassess changes at regular intervals and modify treatments as appropriate.

Pain Treatment History

Many patients with chronic pain have long and sometimes complex treatment histories. Obtain a full history, including:

- Details of treatment success or failure. Ask: "What has worked best to manage your pain?" "What has not worked?"
- Review medication list prior to visit. If medication was trialed previously, why was it stopped? Was there an intolerance? At what dose was each drug tried before labeling as "ineffective"? How long was each drug taken?
- Relevant surgeries, other procedures, and hospitalizations, particularly for pain control
- Perceived origin of pain (work injury, car accident, trauma) and any associated disability or legal actions
- Personal or family history of psychiatric problems, substance misuse, substance use disorder, or other significant medical problems.

Verify these details by reviewing internal records, obtaining outside documentation, and contacting other treating clinicians as necessary.

Quality of Life and Functional Impact

Objective assessment of a patient's function is essential in managing chronic pain. Tools are available to establish functional impact at baseline and progress on functional impact through treatment. For example, the 3-item PEG Scale¹⁸ (Appendix A2) assesses **P**ain intensity, **E**njoyment of life, and interference with **G**eneral activity. This tool is useful to track an individual's function as it changes over time. Therapy should result in the individual's score decreasing. Scores are not directly comparable between patients because individuals vary on which aspect (pain, enjoyment, general activities) is most important.

Comorbid Conditions

The presence of comorbid conditions often impacts treatment decisions.

Medical comorbidities. Obtain a thorough past medical history, with attention to conditions that may raise the risk for harm with pain treatment. Conditions that merit special considerations in pain treatment include sleep disordered breathing, chronic kidney disease, liver disease, cardiopulmonary disease, and neurologic disorders.

For example, obstructive sleep apnea, and other forms of sleep-disordered breathing raise the risk for adverse outcomes and overdose with opioids. Opioids increase the likelihood of central sleep apnea and to a lesser extent obstructive sleep apnea.¹⁹ These effects are compounded when a patient already has sleep-disordered breathing at baseline.

Psychiatric comorbidities. Review the past medical history and assess the presence of psychiatric conditions that could affect the patient's response to chronic pain, communications with the patient about chronic pain, or treatment.

A primary psychiatric condition may contribute to the worsening of chronic pain. Also, psychiatric conditions may develop secondary to chronic pain.

Depression and anxiety disorders are four times more likely among patients with chronic pain than pain-free patients.²⁰ Post-traumatic stress disorder (PTSD) is another common comorbidity.²¹ It is a risk factor for chronic pain^{22,23} and for the transition from acute to chronic pain.²⁴ PTSD in abuse survivors has been linked to increased severity of pain and disability.^{25,26}

Psychiatric comorbidities may affect treatment and referral. Clinicians should be familiar with standard guidelines regarding management of these conditions. (For example, see [Michigan Medicine Depression Guideline](#)). Initial treatment for psychiatric disorders in patients with chronic pain may be influenced by their specific pain syndrome (see non-opioid pharmacologic treatment). If patients do not have an adequate response to therapy, refer them for specialty evaluation, which may involve pain psychology.

Substance use disorders. Obtain a substance use history in all patients with chronic pain, including the use of alcohol, illicit drugs, tobacco, and caffeine. When the etiology of pain is unclear, this history can help assess the risk for substance use disorder prior to considering treatment with opioids. Obtain a family history of substance use disorders as part of a comprehensive risk assessment. Consider use of a standardized screening tool, such as the drug abuse screening test ([DAST-10](#)) or the Michigan opioid risk assessment ([MORA](#)). It is important to document substance use disorders accurately and specify if the substance use is active or in remission. Avoid stigmatizing labels in documentation such as "drug-seeking" or "addict". Instead, use DSM-V diagnostic language. Avoid copying forward progress notes that contain stigmatizing language, or inaccurate information regarding the patient's substance use.

Suicidality. Assess patients with chronic pain for suicidality. Chronic pain is associated with an increased risk of suicidality. In a 2018 study of suicide decedents, 8.8% had evidence of chronic pain, and the percentage increased from 7.4% in 2003 to 10.2 % in 2014. More than half of suicide decedents with chronic pain died of firearm-related injury, and 16.2% died of opioid overdose. These data likely underrepresent the true number of suicide decedents with chronic pain.²⁷

Pain Beliefs and Response to Pain

Pain beliefs and responses to pain may have a positive or negative effect on treatment outcomes. For patients who exhibit negative affect, pain catastrophizing, or other negative pain-specific constructs, consider evaluation by pain psychology. The Chronic Pain Assessment Questionnaire (Appendix A3) evaluates a patient's level of acceptance of their pain, with higher acceptance levels correlating with more successful response to chronic pain management. Self-efficacy and positive treatment expectations can increase resilience and functional outcomes.²¹ Positive cognitive and emotional coping mechanisms can be promoted through multidisciplinary treatment incorporating education, psychological therapies and mindfulness.

Several cognitive constructs and affective responses negatively influence the intensity, distress and dysfunction of the chronic pain experience. Negative affect or emotional distress may be below the threshold for diagnosis of psychiatric disorder (eg, anxiety, depression), yet still have a substantial influence on pain-related outcomes and response to treatment. Negative affect increases the likelihood of transition from acute to chronic pain and is correlated with increased levels of disability, health care costs, mortality, and suicide.²¹ Catastrophizing, where beliefs about the pain experience overwhelm the capacity to function, correlates with negative affect, but also has a unique impact on outcomes, and confers a degree of treatment-resistance.²¹ Fear of pain is closely connected, and leads to a cycle of hypervigilance and avoidance of activity that contributes to negative affect, physical deconditioning, and disability.²¹

Psychosocial Factors

Obtain a thorough social history of interpersonal relationships at home, work, or in other environments that may improve or negatively impact the adjustment to chronic pain. Consider screening patients with chronic pain for a history of trauma and for adverse childhood experiences. In one meta-analysis, individuals with a history of trauma were 2.7 times more likely to have a functional somatic syndrome such as fibromyalgia or chronic widespread pain.²⁸

A variety of psychosocial factors, including patient vulnerability and resilience, influence the development and experience of chronic pain, and affect outcomes such as pain persistence and disability. Functional MRI studies suggest that these psychosocial factors may have neurobiological and structural correlates that impact the central nervous system to either worsen or ameliorate pain.

Cognitive and affective responses may be influenced by spouses or other family members. Spirituality is often overlooked during pain assessment. For many patients, spirituality is an important factor that can influence the experience of chronic pain. Isolation, economic disparities, level of education and access to resources all merit consideration

Physical Exam and Diagnostic Testing

Perform a comprehensive physical exam in patients with chronic pain. Review imaging and other diagnostic testing (x-rays, MRI, EMG, lab studies, etc.). Review urine drug test results. Review the state prescription drug monitoring report (PDMP) report, [MAPS](#) in the state of Michigan).

Arriving at a Diagnosis

After obtaining the history, doing a physical exam, reviewing records and diagnostic test results, assign a diagnosis of chronic pain that identifies:

- The most likely neurobiologic mechanism of the pain: nociceptive, neuropathic, or central sensitization (Table 2).
- Whether it is a primary or secondary chronic pain syndrome.

In some cases, underlying neurobiologic mechanisms may be overlapping, and more than one pain syndrome may be present.

If the diagnosis is uncertain, additional workup may be necessary, including diagnostic testing or specialty consultation. However, even when the underlying pathophysiology is unclear, establish a therapeutic relationship with the patient, and begin developing an individual pain treatment plan.

Designing an Individualized Pain Treatment Plan

Recommendations:

Use shared decision-making to develop an Individualized Pain Treatment Plan that promotes patient self-management.

Preferred therapy is non-pharmacologic or non-opioid pharmacologic and involves multiple modalities.

Avoid long-term opioid prescriptions for chronic pain. Opioids carry substantial risks of harm.

Identify and address clinician and health care system barriers to care.

Steps in creating an Individualized Pain Treatment Plan are outlined in Table 4.

Shared Decisions for Individualized Treatment

A trusting patient-clinician relationship is key to the development of an effective treatment plan for chronic pain. Construct a unique plan for each patient, taking into consideration the individual's experience, circumstances, and preferences. The treatment plan should involve multimodal interventions, promote self-management, and enlist the involvement of a health care team. Use a shared decision-making approach, where patients and clinicians discuss values and preferences, review risks and benefits, and make a decision congruent with patient goals and preferences.²⁹ Frequently reassess and adjust the plan to address barriers to care.

Key to developing an effective treatment plan is a supportive relationship with an empathetic clinician who acknowledges and empathizes with the patient's experience. Set expectations regarding the available treatments for chronic pain. Establish realistic treatment goals for functional improvement or maintenance, not analgesia alone. Inform the patient that finding the right approach may take time.³⁰ Facilitate patient self-management and provide pain psychoeducation (see Appendix H). A team-based approach is helpful in this effort, involving other clinical disciplines such as nursing or behavioral health consultants to provide coaching, education, and support.

A logical rationale for an intervention does not ensure the patient's acceptance and participation in it. A patient's acceptance of therapy is influenced by several complex factors, including characteristics of illness and identity. Patient preferences often favor physical rather than psychological intervention, but gains of psychological therapies may exceed patient expectations.³¹

Preferred Interventions

Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for the treatment of chronic pain.¹¹ There is insufficient evidence to support the use of long-term opioid use for chronic pain. Opioids carry substantial risks of harm. Use shared decision-making to choose treatment interventions. A single intervention is unlikely to be fully effective for chronic pain, since chronic pain is a complex disease process with multiple contributing biopsychosocial factors. Combining several modalities, and emphasizing self-management is most effective.³² (Figure 1)

Clinician and Health Care System Barriers

When patients with chronic pain feel judged or scorned by health clinicians, this stigma can be a significant barrier to effective care. Similarly, clinicians caring for patients with chronic pain often experience negative emotions such as frustration, lack of appreciation, and guilt.³⁰

Patients and clinicians alike encounter frustration when confronted with barriers within the health care system. Common barriers include difficulty in accessing care, limited time for visits, and inadequate reimbursement for evidence-based treatments.

A team-based approach, adequate consultative support, and training can begin to address some of these barriers. Patients may have individual barriers to accessing care or participating in self-management. Provide them with specific support as needed.

Assess cognitive and verbal ability

For patients with cognitive and/or verbal disability, when analgesic plan involves a caregiver, caregivers should receive additional education on pain assessment. Providers should also carefully assess function and goals

with both patient and caregiver.

- Assess fall risk, cognition, respiratory status, and risk for sleep disordered breathing prior to prescribing opioids.
- Reduce the initial dose of opioids by 25-50% and titrate slowly to avoid over sedation.
- Consider using a non-verbal pain scale such as CPOT (Critical Care Pain Observation Tool) or FLACC (Face, Legs, Activity, Cry, and Consolability) to assess efficacy of pain medications.
- Exercise universal precautions for controlled substance prescribing and limit pill count for patients at risk of having their medications diverted
- Schedule frequent follow up with patients
- Consider random urine drug screen (UDS)
- Consider pill counts
- Emphasize the importance of keeping medications secure and locked to care provider/home manager.
- Provide disposal information for unused pills
- Ensure caregiver receives education on appropriate Intranasal Narcan use and administration to the patient if indicated

Health inequity and disparity

Many patient populations are unintentionally marginalized by both health care providers and health systems. This inequity is especially true with regard to pain management amongst non-white Hispanic, black, and other minority populations.^{33,34} Several factors should be considered when treating these vulnerable patients. It is the provider's responsibility to recognize that inequity in this area is due in part, but not limited to, systemic barriers and complex influences such as implicit biases unbeknownst to providers. For example, patients with sickle cell disease frequently report difficulties in obtaining adequate pain relief from providers during a vaso-occlusive crisis. In this vulnerable population, studies have shown delays in administering pain medications due to accusations of drug seeking behavior, exaggeration of pain, and uninformed or negative attitudes held by providers concerning sickle cell disease.³⁵

To diminish these inequities surrounding pain management, providers should attempt to remove as much individual discretion from decision making as feasible. When possible, providers should utilize resources such as: checklist, guidelines, or system protocols to avoid the influences of implicit biases on their management. Providers need also recognize access limitations faced by patients and ensure any treatment regimen or follow-up planning is readily accessible. An important consideration is to involve these patients in shared decision making while offering all available treatment options to circumvent and mitigate any healthcare related obstacles these patients may encounter. Alternative options should then be explored based on individual circumstances.

Non-Pharmacologic Treatment

Recommendations:

Lifestyle management. For all patients, recommend:

- Regular exercise. Start small, gradually increase to at least 150 minutes/week at moderate intensity. Adjust this goal to the individual's status.
- Teach good sleep habits. Screen for sleep disturbance. Consider sleep quality, post sleep evaluations, and sleep disordered breathing.
- A Mediterranean pattern of eating to lower inflammation and maintain a healthy weight.

Physical modalities:

- Consider physical therapy when patients have functional deficits or secondary pain generators.
- Consider massage therapy as part of a multimodal treatment plan.

Behavioral health interventions. Evidence-based interventions include mindfulness-based stress reduction, cognitive behavioral therapy, acceptance and commitment therapy, and self-regulatory and psychophysiological approaches (eg, biofeedback, relaxation training, hypnosis). See Appendix H.

- Refer patients with significant psychological issues (eg, comorbid psychiatric condition, previous trauma, challenges in managing and coping) to a psychologist or therapist.
- Consider referring any patient with chronic pain to a psychologist or therapist to address the psychological effects of chronic pain.

Integrative medicine:

- For interested patients, consider combining or coordinating historically non-mainstream practices that are evidence-based (eg, acupuncture, herbal supplements) as part of a multimodal treatment regimen.
- Evidence regarding the benefits and harms of marijuana for chronic pain is insufficient to recommend its use. Limited data support that using cannabidiol (CBD) alone is safe.

Non-pharmacologic options for treating chronic pain are summarized in Table 5.

Lifestyle Management

Exercise. For all patients recommend regular exercise as a component of multimodal treatment. Decrease the patients' fear of movement. Encourage a progressive aerobic exercise program with a goal of at least 150 minutes of moderate-intensity exercise weekly. Adjust this goal for each individual's physical status.

Exercise is structured, repetitive, physical activity to improve or maintain physical fitness. In patients with chronic pain, exercise improves both function and chronic pain symptoms, in addition to overall health and quality of life. Forms of exercise that have been studied include aerobic exercise, resistance-based exercise, water-based exercise, and styles of exercise such as yoga (for chronic primary musculoskeletal pain³⁶), tai chi (for chronic primary musculoskeletal pain, osteoarthritis, osteoporosis, neck pain³⁷), and Pilates (for chronic primary musculoskeletal pain neck pain, osteoporosis³⁸). Studies vary considerably in mode of exercise, content of program, frequency, and duration of activity. In most studies, the frequency of exercise was between 1-5 times per week, averaging 2-3 times a week. Another factor was whether activities were performed in supervised sessions or as home exercises, with home exercises potentially increasing the frequency of the activity. Prescribed exercise was generally moderate to moderately-high in intensity. No one type of exercise has been shown to be superior to another in all patient populations.

Sleep. For all patients recommend good sleep habits. Screen for sleep disturbance. Sleep complaints occur in 67-88% of individuals with chronic pain. Sleep and pain are often linked. Sleep disturbances may decrease pain thresholds and contribute to hypersensitivity of neural nociceptive pathways. Conversely, pain may disturb sleep. Nonpharmacologic sleep treatments are associated with improved fatigue and sleep quality. However, the effect on pain is comparatively modest and short-lived.

Diet. Recommend a Mediterranean pattern of eating to lower inflammation and maintain a healthy weight. Although inflammation is part of the nociceptive process, research into the role of diet in modifying

inflammation is in its early stages. The Mediterranean pattern of eating, characterized by a high intake of fruits, vegetables, whole grains and an emphasis on omega-3 fatty acids, has been established as a dietary pattern that lowers inflammation especially in the setting of cardiovascular disease.³⁹ Emerging evidence shows connections between the Mediterranean pattern, lowered inflammation, and improvement in pain and function in osteoarthritis.⁴⁰

Physical Modalities

Physical therapy. If patients have functional deficits or secondary pain generators that directed therapy may improve, refer them to physical therapy.

The goal of physical therapy is to improve function. Therapeutic exercise, other modalities, manual techniques, and patient education are part of a comprehensive treatment program to accomplish this goal.

- Modalities such as hot packs, ice, ultrasound, transcutaneous electrical nerve stimulation (TENS), iontophoresis, and traction may decrease pain and increase tissue extensibility, thereby facilitating stretching and mobilization. Table 4 reviews selected modalities.
- Manual therapy helps optimize proper mobility, alignment and joint biomechanics.
- Therapeutic exercise consisting of stretching, strengthening, conditioning, and muscle re-education is useful in restoring joint range of motion, muscle strength, endurance, and to correct muscle imbalances.

Evidence is limited regarding the long-term benefit of any single individual treatment modality. However, they may be used as part of a multimodal treatment program to improve function, quality of life, and alleviate pain.

The basic components of a physical therapy prescription include:

- Diagnosis for which therapy is being prescribed.
- Therapeutic protocol for treatment, including therapeutic exercise, other modalities, and manual techniques to be employed or tried.
- Duration and frequency of desired therapy.
- Precautions.

When treatment goals have been met or when progress plateaus, formal therapy may be discontinued, but advise patients to continue with a program of independent daily home exercise.

Transcutaneous electrical nerve stimulation (TENS). Consider TENS either along with physical therapy or as an adjunct to multimodal treatment. TENS applies low voltage electrical stimulation using skin contact electrodes. Proposed mechanisms of action include gate control theory, endorphin theory, and augmentation of descending inhibition. Evidence is limited for the efficacy of TENS in pain management.⁴¹ However, it is relatively safe, with units relatively available and easy to use.

Do not use TENS near implanted or temporary stimulators (eg, pacemakers, intrathecal pumps, spinal cord stimulators), near sympathetic ganglia or the carotid sinus, near open incisions or abrasions, over thrombosis or thrombophlebitis, or in pregnancy. Use caution with patients with altered sensation, cognitive impairment, burns, malignancy, or open wounds.⁴¹

Massage therapy. Consider massage therapy as part of a multimodal treatment plan. Massage therapy is manual manipulation of muscles and connective tissue to enhance physical rehabilitation and improve relaxation. It can reduce pain scores for patients with low back pain,⁴² knee osteoarthritis,⁴³ juvenile rheumatoid arthritis,⁴³ chronic neck pain,⁴³ and fibromyalgia.⁴² Not yet determined are the optimal number, duration and frequency of massage sessions for treating pain.

Behavioral Health Approaches

Refer patients with significant psychological issues (eg, comorbid psychiatric condition; previous physical, emotional, or sexual trauma; challenges in managing and coping) to a psychologist or therapist. Consider referring any patient with chronic pain to a psychologist or therapist to address the psychological effects of chronic pain. These interventions can be successful regardless of the patient's baseline status.

Current psychological interventions for chronic pain are based on recent advances in our understanding of the complexity of pain perception. Pain is influenced by a wide range of psychosocial factors, such as emotions, sociocultural context, and pain-related beliefs, attitudes and expectations.

Chronic pain that persists for months or years often initiates a progressive loss of control over numerous aspects of one's psychological and behavioral function. A biopsychosocial model is now the prevailing paradigm for interventional strategies designed to treat chronic pain. This model places an emphasis on addressing cognitive-behavioral factors pertinent to the patient's pain experience.

The strong evidence for the contribution of psychosocial factors in pain experience, particularly in explaining disability attributed to pain, has led to the development of multidisciplinary pain rehabilitation programs (MPRPs) that simultaneously address physical, psychological, and functional aspects of chronic pain disorders. For some patients, referral for individual behavioral and psychological intervention may be all that is required.

Cognitive behavioral therapy (CBT). The way patients think about themselves, others, and the future can have a major impact on their moods, behavior, and physiology. The two main tenants of CBT approaches to chronic pain are:

- The feeling of pain and the emotional, physical, and social impact of pain are interrelated, but can be separated for treatment purposes. Therefore, problems with functioning related to pain can be addressed even if pain is not targeted directly and remains unchanged.
- Psychological factors can influence the experience of pain itself.

Cognitive restructuring involves several steps that help to modify the way in which patients view pain and their ability to cope with pain. Treatment approaches that incorporate these principles can produce significant benefits, such as reduced pain, improved daily functioning, and improved quality of life.^{44–48}

Mindfulness-based stress reduction. Mindfulness is a process of openly attending, with awareness, to one's present moment experience.⁴⁹ Mindfulness aims to empower patients to engage in active coping by encouraging them to be aware of the present, where difficult thoughts, feelings, and sensations are acknowledged and accepted without judgement.⁵⁰

Mindfulness based stress reduction (MBSR) may improve pain function in people with chronic pain. MBSR can provide patients with long-lasting skills effective for managing pain.³⁴ Strong evidence shows that MBSR reduces functional disability and improves pain management for a variety of chronic pain conditions including low back pain,⁵¹ fibromyalgia, rheumatoid arthritis, and patients with opioid misuse. The most studied intervention uses an 8-week format of 2-hour/week classes, a 6-hour day in the middle, and daily at-home audio recordings.

The mechanism of action for mindfulness-based strategies is unknown. It seems to be multifactorial, including both physical changes in the stress response system that drive markers of inflammation, as well as psychological mechanisms such as stress resilience and coping.⁵²

Acceptance and commitment therapy (ACT). ACT is a form of CBT. In some cases, trying to control or

change pain and thoughts about pain can be counterproductive. ACT is an alternative way to increase acceptance of some of the aspects of chronic pain that may be difficult to alter. Acceptance may free individuals to pursue activities in line with their values.⁵³ The ACT clinical model has six core processes:

- A. Acceptance of events and your feelings around them.
- B. Perceiving things as they are.
- C. Being present and mindful.
- D. Observing yourself in context.
- E. Identifying personal values.
- F. Setting goals based on your values and committing to actions in accordance with those goals.⁵⁴

Various methods of delivering ACT have been shown to be effective in treating chronic pain⁵⁵ either as an individual face-to-face intervention,^{56,57} a group-delivered face-to-face intervention,^{58–66} via self-help books,^{67,68} or through an internet-based delivery.^{69–73} ACT based therapy has been shown to decrease pain, improve function, and improve quality of life.

Self-regulatory and psychophysiological approaches. The experience of chronic pain elicits strong physiological reactions that are often accompanied by cognitive thoughts and processes. Several simple techniques harness the connection between the mind and body to improve awareness of and increase control over both psychological and physiological responses to pain.

Techniques include biofeedback, relaxation training, and hypnosis. Biofeedback provides real-time information about physiological processes (eg, heart rate, respiratory rate, muscle tension) with a goal of increasing voluntary control over them. It is often coupled with relaxation training (deep breathing or conscious focusing on relaxation). Biofeedback can decrease the frequency of pain, improve self-management, and decrease use of analgesic medications in both migraine and tension type headaches in adults and adolescents.^{74,75} Hypnosis is a state of increased attentional awareness leading to a state of increased relaxation. It has been examined in a variety of pain conditions and found to be effective in decreasing pain most pain conditions, with a reduction in overall pain between 29–45%.^{76,77} Effects of specific analgesic hypnotic suggestion were strongest in individuals of high to moderate suggestibility. Most people fall within those two categories, indicating a majority of people would benefit.⁷⁶ A 2020 meta-analysis indicates a possible role for hypnosis in decreasing opioid medication, with hypnosis moderately reducing pain levels coupled with small reductions in opioid dosing.⁷⁸

Integrative Medicine

For interested patients, consider adding historically non-mainstream practices that are evidence-based as part of a multimodal treatment regimen. As evidence emerges regarding the biological role of these treatments, their utility may change.

Integrative medicine is an approach that combines and coordinates conventional medicine with evidence-informed practices that historically are not mainstream. Emerging evidence suggests a role for many less conventional treatments in the management of chronic pain due to their benefits and safety compared to opioid therapy. In addition to previously noted treatments (massage, yoga, tai chi, mindfulness), accumulating evidence supports the use of acupuncture and herbal supplements. More information may be found at the Center for Complementary and Integrative Health at <https://nccih.nih.gov/>.

Acupuncture. Acupuncture in traditional Chinese medicine uses the insertion of needles into specific areas to manipulate anatomical energetic meridians. The nature of the psychological effect continues to be debated,

but efficacy has been established for many chronic pain conditions.⁷⁹ The best evidence exists for osteoarthritis, chronic neck and low back pain, fibromyalgia, and headache. Treatment frequency varies, with the most commonly cited being 1-2 times per week for 4-8 weeks. Some studies show effects lasting 6-12 months.⁸⁰

Herbal supplements. Patients frequently request information about herbal supplements. The evidence for the use of some supplements is growing. Many are safe and may be considered when patients are interested. See Table 6.

Marijuana. Evidence regarding benefits and harms is currently insufficient to recommend using "medical" marijuana for chronic pain. Some data support cannabidiol (CBD) alone as being relatively safe.

With an increasing number of states legalizing marijuana, clinicians and patients are asking about the use of cannabinoids to treat a variety of conditions. The cannabis plant produces many phytocannabinoids, with the highest concentration of these being tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is the molecule with psychoactive properties that appears to be responsible for most adverse effects. This remains a challenging and complex area to address. Regulatory and historical factors have resulted in very limited evidence concerning the endocannabinoid system and cannabis pharmacology.

Systematic reviews have found that cannabinoids may be modestly effective for some chronic pain, primarily neuropathic pain, based on limited evidence.^{43,44} However, the evidence is largely based on studies of high THC-containing products, which also show high rates of adverse events, such as sedation and psychomotor impairment. In the absence of regulation, the potency and composition of cannabis products are highly variable. Due to these factors, evidence is currently insufficient to recommend using marijuana for relief of chronic pain.

As new evidence begins to emerge regarding the possible role of CBD in analgesia and anti-inflammatory pathways, we may see a role for CBD alone or for products with a high CBD: THC ratio in chronic pain.^{81,82} For patients wishing to use CBD alone, some data support CBD as being relatively safe, although there are some potential cytochrome P450 metabolism interactions that should be reviewed. In 2018 the US Drug Enforcement Administration (DEA) reclassified the CBD-based product Epidiolex as Schedule V, which is the least restrictive schedule; however, it is only approved or studied in the setting of two forms of rare seizure disorder. CBD is not recommended for first-line therapy for the treatment of chronic pain. However, patients who have failed other treatments or are opioid dependent may be started on low (5-10 mg twice daily) doses, with slow increases of dose.⁸¹ Of note, these products are not regulated and therefore it is unclear how to determine dose or quality so these products should be considered with caution.

Non-Opioid Pharmacologic Treatment

Recommendations:

Consider prescribing systemic or topical non-opioid medications as an adjunct to the non-pharmacologic treatments noted above. Medications often have limited effectiveness, significant interactions or toxicity, and may promote false beliefs about the benefit of medications.

Select medications based on:

- Known effectiveness for specific pain mechanisms (nociceptive, neuropathic, central sensitization)
- Potential to treat comorbid disorders, such as insomnia or mood disorder.

Prescribe an adequate trial of days to weeks of scheduled dosing. Avoid as-needed medication use. Discontinue all ineffective medications to avoid polypharmacy, minimize toxicity, and limit unrealistic

beliefs about the benefit of medications.

Several classes of medications can be part of effective chronic pain management, including acetaminophen, non-steroidal anti-inflammatory medications (NSAIDs), anticonvulsants, serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), muscle relaxants, and topical agents. Other non-opioid medications (eg, certain antidepressants and anticonvulsants) may simultaneously treat comorbid problems (eg, mood disorder, insomnia). Classes of non-opioid medications used for chronic pain and their potential benefits and harms are summarized in Table 7.

A successful regimen may combine low doses of different types of pain medications to treat different mechanisms of perceived pain simultaneously, increasing medication effectiveness while limiting the risk of toxicity.

- Primary pain syndromes such as chronic widespread pain (eg, fibromyalgia), headaches, and primary visceral pain (eg, irritable bowel syndrome) may respond to SNRIs, TCAs or anticonvulsants.
- Neuropathic pain may respond to those classes of medications as well as some topical agents.
- Nociceptive pain may respond to acetaminophen, NSAIDs, muscle relaxants, or topical agents.
- Neuropathic pain may respond to SNRIs, TCAs, anticonvulsants, or topical agents.
- Central pain syndromes such as chronic widespread pain (eg, fibromyalgia), headaches, and primary visceral pain (eg, irritable bowel syndrome) may respond to SNRIs, TCAs, or anticonvulsants.

Acetaminophen. Acetaminophen may occasionally be a useful medication to treat mild to moderate chronic pain, whether given as needed ("PRN" dosing), or at scheduled intervals. When combined, an NSAID and acetaminophen can be synergistic and equal to or more effective than acetaminophen plus an opioid.⁸³

For healthy people, avoid total acetaminophen doses > 3 g/day (2 g/day in patients with chronic liver disease). Acetaminophen may cause small increases in the risk for upper gastrointestinal bleeding and small elevations of blood pressure.⁸⁴

Non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs are among the most widely used medications in the US. Long-term NSAID therapy for chronic pain may benefit some patients, particularly those with defined pain generators and who are at low risk for complications. For low back pain, use of an oral NSAID is somewhat more effective than placebo for analgesia,⁸⁵ but only slightly for disability. Celecoxib is more effective in low back pain than acetaminophen, but the effect is modest.⁸⁶

Chronic NSAID use poses significant risks for gastrointestinal bleeding, acute kidney injury or chronic kidney disease, and platelet dysfunction. Older age adds particular risk. Older adults receiving daily NSAIDs for six months or more face a 6-9% risk for upper gastrointestinal bleeding requiring hospitalization. For high risk patients for whom NSAIDs have proved to be the only effective treatment, consider proton-pump inhibitors for upper gastrointestinal prophylaxis.

NSAIDs may also increase risk for exacerbations of hypertension, heart failure, and chronic kidney disease. NSAID use in patients with heart disease or its risk factors increases the overall risk of heart attack or stroke.

Serotonin-norepinephrine reuptake inhibitors (SNRIs).

SNRIs (duloxetine, venlafaxine, or milnacipran) can benefit patients with a variety of pain syndromes, including non-specific low back pain, neuropathic pain of various origins, functional abdominal pain, and central pain syndromes such as fibromyalgia. For low back pain, duloxetine at doses up to 120 mg/day reduced both non-specific and neuropathic symptoms. Its mechanism of action seems to be independent of any antidepressant effect. SNRIs are somewhat more effective for functional abdominal pain than tricyclics.⁸⁷ Duloxetine is FDA-

approved for diabetic neuropathy and fibromyalgia, though it improves pain scores more than function.

SNRIs are generally well-tolerated, but discontinuing an SNRI requires a gradual tapering down of the dose to avoid withdrawal symptoms, which can occasionally be severe.

Anticonvulsants. Anticonvulsant medications such as gabapentin, pregabalin, and topiramate can be effective for treating neuropathic pain. Dosing can be complex. They have significant adverse effects and are often only modestly effective. Additionally, use topiramate with caution in reproductive-aged women because it increases the risk of cleft lip and cleft palate in newborns.

Pregabalin is approved for the treatment of diabetic neuropathy and fibromyalgia, though it improves pain scores more than function. Gabapentin has only minor benefit in chronic daily headache or migraine. It is not effective in chronic non-specific low back pain.^{61,88} Gabapentin and pregabalin are not effective in acute low back pain.

Older anticonvulsants such as carbamazepine and phenytoin have some efficacy for neuropathic pain, but are associated with frequent adverse effects, drug-drug interactions and potentially severe adverse reactions, such as granulocytopenia and hyponatremia.

Pregabalin is a federal Schedule V controlled substance, and gabapentin has been scheduled in many states. Both of these medications produce an increased addiction risk. When combined with opioids, they have been associated with a small increase in death rate. Advise patients treated with gabapentin or pregabalin about increased appetite and the potential for rapid and marked weight gain.

Topiramate at higher doses has been associated with significant speech and cognitive effects

Tricyclic antidepressants (TCAs). TCAs may be potentially useful in a variety of pain syndromes, particularly in neuropathic pain and headaches. They also may benefit comorbid disorders such as insomnia, anxiety, depression, panic disorder, and even smoking cessation efforts. TCAs may have particular use in neuropathic pain, vascular headache prophylaxis, and centralized pain syndromes such as fibromyalgia. Trial data suggest only a modest benefit in functional abdominal pain and less benefit than SNRIs.⁸⁹ In chronic low back pain, low dose TCAs resulted in somewhat less disability at 3 months but had less effect at 6 months.⁹⁰

Doses required for pain treatment are lower than for mood disorders. The lower doses generally avoid problems such as QT prolongation. For patients with sleep initiation problems, taking a TCA at dinnertime rather than bedtime may reduce problems with sleep initiation and with morning fatigue.

When a TCA is used for pain or mood, the time needed for a response can be days to weeks.

TCAs may have adverse effects that can limit their usefulness, such as anticholinergic effects and dysrhythmias. Caution patients about enhanced appetite and the potential for weight gain. Constipation prophylaxis may be needed.

Muscle relaxants. Sedating or non-sedating muscle relaxants are often prescribed for chronic myofascial pain, despite little or no evidence for a long-term benefit.⁸⁸ Cyclobenzaprine, tizanidine, and metaxalone can cause significant sedation, while methocarbamol is less likely to do so. Benzodiazepines pose a significant risk for long-term dependence and misuse, and they substantially increase the danger of overdose when used together with opioids. Baclofen, while somewhat useful for spasticity, has little role as a muscle relaxant, poses a significant risk for dependence, and should generally be avoided.

Topical agents. Topical NSAIDs and anesthetics are occasionally useful in nociceptive or neuropathic pain syndromes. They can be expensive and are often not covered by insurance.

- Topical NSAIDs benefit a minority of osteoarthritis patients. They generally are not useful in other types of pain.^{91–93}
- Topical lidocaine patches (prescribed or over-the-counter) can be effective. Ointment is less effective and can be messy. Both are expensive and often not covered by insurance. Over the counter 4% lidocaine cream is not expensive, but only marginally effective.
- Capsaicin cream (1%, not 0.25%) can be modestly effective, is available without prescription, but requires care in application to avoid unwanted burning. Compounded capsaicin 8% cream is more effective, but the cost may be prohibitive.
- When other treatments have failed, topical nitroglycerin may have some effect for wound pain, anal fissure pain, vulvodynia, and diabetic neuropathy.
- Compounded topical 5% morphine can provide local wound analgesia and may promote healing. It is only available at compounding pharmacies and can be expensive.

Systemic effects of topical agents are generally minimal. Headache can complicate treatment with nitroglycerin. Avoid nitroglycerin in patients who use phosphodiesterase type 5 inhibitors (avanafil, sildenafil, tadalafil, vardenafil) for erectile dysfunction.

Opioids: Decision Phase

Recommendations:

Assess factors that indicate whether opioids may be beneficial.

Consider potential risks of opioids:

- Potential risks of opioid use for all patients include: physical adverse effects; cognitive impairment; social, personal, and family risks; failing urine screening; potential for opioid misuse.
- Special populations – Patients with factors such as older age, pregnancy, lactation, or chronic illness have higher risks associated with opioid use (Table 8).
- Benzodiazepines – Generally do not initiate opioid therapy in patients routinely using benzodiazepine therapy. Both increase sedation and suppress breathing.
- Marijuana – Discourage concomitant use of THC- containing marijuana products and opioids. Marijuana's adverse effects may compound those of opioids.

Assess the benefits and risks to determine whether an opioid will improve overall chronic pain management.

Decide whether to recommend adding an opioid to treatment.

Considerations for Opioid Use

Deciding whether to prescribe opioids is based on an assessment of benefits and harms. While opioids should never be the main treatment for chronic (or acute) pain, in some circumstances, opioids may complement other therapeutic efforts. Important considerations and branching decisions are illustrated in Figure 1 for opioid naïve patients and Figure 2 for patients already on opioids.

Potential Benefit

Assess factors that indicate whether opioids may be beneficial. Based on pain assessment, characterize the patient's pain based on:

- **Time frame:** acute, subacute, or chronic.
- **Mechanism:** nociceptive, neuropathic, central, or a combination of these. Many pain states are the result

of a "mixed picture."

- **Pain generators:** list each painful area and determine each pain generator.
- **Approximate percentage:** establish the percentage of pain each pain generator is contributing to the overall clinical status.

A careful history can indicate the types of pain involved and guide treatment plans. For example, if NSAIDs provide significant relief, an inflammatory component to pain is likely. Note whether other modalities and medications have helped or not, and incorporate that information into the treatment plan. Use past experience to guide the decision to start membrane stabilizers (anticonvulsants) and other non-opioid therapies and to determine initial doses. As with all medical decisions, carefully consider risks and benefits.

Short-term opioid therapy may be appropriate for acute pain management to allow for rehabilitation. For chronic pain, opioid therapy is beneficial if it allows a return to function or maintenance of function with minimal adverse effects. If patients are not meeting functional goals during the course of therapy for nonmalignant pain, opioid therapy has failed and should be discontinued.

Potential Risks

Review the patient's risks and determine if opioid-based therapy is likely to result in harm.

General risks. Potential risks for all patients include:

- **Physical adverse effects.** Common opioid adverse effects include nausea, constipation, pruritus, respiratory depression, and hot flashes. Chronic opioid use can alter endocrine function and may also lead to dry mouth and subsequent dental caries.
- **Cognitive impairment.** Patients new to opioids should not drive a vehicle or operate power equipment or heavy machinery until they see how they are impacted by the therapy.
- **Social, personal, and family risks.** Being an opioid user carries a risk for social stigma. Additional risks are inherent to possessing opioids, including becoming a target for home invasion. Insecure storage may put other family members and pets at risk for opioid poisoning.
- **Failing urine drug screening tests.** Some jobs require a negative urine drug screen, and employment may not be compatible with opioid therapy. Patient can be harmed financially and professionally if they screen positive for an opioid, even when prescribed and monitored by a clinician.
- **Potential for opioid misuse or opioid use disorder.**
 - Patients with depression, anxiety, or a history of substance use disorder are at risk.
 - Patients with active alcohol use disorder, illicit drug use, or a history of these problems are at risk.

Special populations. Older age, pregnancy, lactation, and chronic illness can impact the safety of opioid medications, so use extra caution with these patient populations. Specific considerations are outlined in Table 8.

Benzodiazepine and opioids – a safety concern. Generally, do not initiate opioid therapy in patients routinely using benzodiazepine therapy. Both drugs are sedating and suppress breathing. Together they can cause a fatal overdose.

In select cases, co-prescribing may be warranted, such as use of a benzodiazepine for an MRI. In those cases, discuss the risks with the patient. Furthermore, consider the kinetics of each drug relative to the timing of procedures. For example, counsel patients taking hydrocodone daily to skip a dose if they need to take a benzodiazepine for an MRI; benzodiazepines and short-acting opioids should not be taken within two hours of each other. When clinicians inherit patients who are co-prescribed sedatives and opioids, carefully review the relative benefit of each medication and prescribe intranasal naloxone. Consider discontinuing one of the

medications.

Marijuana, CBD, and opioids. Discourage concomitant use of THC-containing marijuana products and opioids. The adverse effects of cannabis products may compound similar effects with opioids, leading to safety concerns. Evidence about the combined use of cannabis and opioid prescriptions is limited and inconclusive at present.⁹⁴ If opioids are otherwise indicated, current evidence is insufficient to recommend against prescribing opioids to patients using CBD alone.

Opioid Risk/Benefit Decision

As with all medications, consider the risks and benefits of prescribing an opioid.

Expected functional benefits of opioid use should be clear, with the continuation of opioid therapy dependent on achieving them. While improved sleep and mood are somewhat subjective and should be noted, seek more objective evidence of benefit in order to prescribe and continue opioid therapy. Consider the ability to walk farther, exercise longer, work more, etc. Before initiating opioid therapy, ask patients to identify the functional goals they wish to achieve with opioid therapy, then see if they are meeting these goals at follow up.

Occasionally opioids may have less risk than other pain management medications. Examples include patients vulnerable to gastrointestinal bleeding for whom NSAIDs are contraindicated and patients experiencing cognitive effects from membrane stabilizers.

Opioids: Initiation and Treatment Phase

An overview of prescribing opioids in opioid naïve patients is presented in Figure 1.

Drug Selection and Dosing

Recommendations:

In selecting opioids, consider patient factors:

- History with opioids: opioid naïve or opioid tolerant
- Previous opioids used
- Special population factors (eg, older age, pregnancy); see Table 8
- Need for accompanying naloxone prescription.

Dosing:

- For initial daily doses, start with a short-acting opioid, and do not exceed 20 MME/day (oral morphine milligram equivalents per day).
- For up titration over time, do not exceed 50 MME/day.

Assess initial responses frequently. See the patient every 1-4 weeks. Titrate the dose and assess response within 2-6 weeks.

When the benefits of adding an opioid to other therapy outweigh the risks, select the initial drug and dose based on the:

- **Patient:**
 - Opioid naïve or opioid tolerant (ie, has been on ≥ 60 MME/day or 25 mcg/hour transdermal fentanyl for ≥ 7 days)

- Patients previously treated with opioids
- Special populations affecting dosing
- **Drug:**
 - Duration
 - Potency
 - Delivery mechanism

All opioids are essentially similar regarding effects and adverse effects. True allergy to any of them is very rare. Morphine and codeine may be slightly less well tolerated, but can be used unless adverse effects become intolerable or a medical contraindication is present.

Opioid naïve patients. In these patients, start with a short-acting opioid at a dose of ≤ 20 MME/day. Over time, the dose may be cautiously titrated. Do not exceed a daily dose of 50 MME.

Opioid tolerant patients. Morphine is the default choice, unless contraindicated. Morphine can be prescribed by all routes, unlike oxycodone. It has a straightforward dose calculation with a predictable analgesic interchange and conversion between parenteral and oral dosing. It is available in long-acting preparations. Cost of all forms of oral morphine is lower, and the long-acting form is covered by all insurances, including Medicaid. The maximum daily dose should not exceed 50 MME. For any doses > 90 MME/day, document the medical justification.

Another option for opioid tolerant patients is buprenorphine, transdermal or buccal. Compared to full agonist therapy, buprenorphine has no ceiling on respiratory depression, generally provides good analgesia, gives consistent serum plasma levels, and does not lead to hyperalgesia or tolerance with the same frequency. Transdermal buprenorphine dosed at 5 mcg/hr (one patch per week) is approximately equal to 20 MME/day. Starting doses of buccal buprenorphine would be 75 mcg once or twice/day. Unfortunately, these options may not be covered by some insurances such as Medicaid.

Transdermal buprenorphine takes approximately 12-24 hours to reach a steady state, during which a short-acting oral opioid may be needed for one-half to a full day, and then should be discontinued. Advise patients to rotate patch locations to avoid skin breakdown. If a rash occurs due to contact with the adhesive, minimize this problem by applying a medium-strength topical steroid such as 0.1% triamcinolone cream to the area 2 hours prior to placement of the patch.

Previous opioids used. If a patient is on multiple opioids, convert to a single opioid when possible. For patients treated with short-acting medications, convert to or add a long-acting medication using the equianalgesic dosing (MME/day) and conversion information in Appendix C. Once the patient is on a long-acting opioid, the short-acting opioid should generally be discontinued.

Dosing for special populations. Older age, pregnancy, lactation, and chronic illness impact the safety of opioid medications, opioid choice, and dosing. Specific considerations are outlined in Table 8.

Naloxone indications. Patients with medical conditions impacting the heart, lungs, or central nervous system are candidates for intranasal naloxone as a rescue strategy. Any patient, regardless of medical comorbidity, who is on > 50 MME/day should also have intranasal naloxone prescribed. Educate family and friends on how and under what circumstances to administer the intranasal naloxone. If a patient is taking benzodiazepines or uses other sedating medications, discuss the risks, prescribe intranasal naloxone, and consider tapering down the opioid dose or converting to an alternative analgesic strategy.

Drug duration and conversion to long-acting preparations. Limit short-acting opioid use over time. If pain persists beyond a few weeks and opioid use is thought to be beneficial, or requiring continuation of greater

than 20-30 MME/day, consider converting to a long-acting preparation. Long-acting preparations provide more stable serum levels and slow the development of opioid tolerance. Short-acting opioids used over time result in tolerance more rapidly than long-acting opioids.

Breakthrough Pain. During dose titration, short-acting medication may be provided for breakthrough pain, but should soon be discontinued. In general, when long-acting opioid preparations are prescribed, use of a short-acting opioid should be a few times per month or not at all. Breakthrough dosing should not occur in multiple daily doses. The only exception is during the first few days of titration, when the long-acting medication is being adjusted to a proper steady state dose. This generally takes 3-5 half-lives of the medication.

Frequent initial assessments. Initially see the patient frequently (every 1-4 weeks) to assess their response to the opioid treatment, monitor for adverse effects, assure compliance, and assess for any inappropriate use or behavior. Reminders of the terms of the treatment agreement are useful in this stage.

Reassess the plan in as soon as 2-6 weeks. Keep the dose titration phase relatively short. If after 2-6 weeks, the patient has not achieved satisfactory pain control with a stable dose of medication, refer the patient to a pain management specialist. It is also reasonable to consider discontinuation of opioids at this point, assuming that adequate dosing was given. Opioids do not effectively treat all patients.

Methadone, Buprenorphine, and Fentanyl

Recommendations:

Methadone

- Only clinicians with experience with methadone should prescribe it.
- Do not use methadone as first-line treatment for chronic pain.
- Consider methadone for its prolonged duration of effect, which is useful for longer term therapy and minimizes euphoria with low doses.
- Avoid prescribing methadone in combination with other controlled substances.

Buprenorphine

- Consider buprenorphine when a safer, lower side-effect profile medication is preferred over full agonist opioids or for patients with tolerance to other opioids.
- Consider its higher expense.
- Be familiar with transdermal and buccal buprenorphine. Sublingual buprenorphine should be initiated only by prescribers trained in its use. It can provoke acute opioid withdrawal if not done correctly.
- Buprenorphine can be prescribed for pain without an XDEA waiver, but the waiver is required to prescribe medication-assisted therapy for opioid use disorder.

Fentanyl

- Do NOT consider fentanyl for opioid naïve patients.
- Consider prescribing fentanyl in only a few unusual situations (see text).
- Do NOT use transdermal fentanyl over a long period because opioid tolerance develops quickly.

These three drugs have special properties and uses deserving special description.

Methadone. Do not use methadone as first-line treatment for chronic pain. Before a clinician prescribes methadone, the clinician should have gained experience monitoring and prescribing it, or should consult a pain specialist.

Special safety hazard and unique advantages. Methadone is unique among opioids, with both increased

safety concerns and advantages in long-term therapy. The safe use of methadone requires knowledge of its particular pharmacologic properties. Methadone's duration of adverse effects far exceeds its analgesic half-life, making it dangerous when combined inappropriately with other controlled substances. Methadone may be useful for patients who require prolonged opioid therapy because it does not tend to require increasingly large doses over time (tolerance). Methadone is also available at relatively low cost.

Many patients are aware that methadone is often associated with opioid addiction therapy. Patients may need additional counseling that methadone is an effective analgesic, not merely a treatment for opioid addiction.

Longer duration affects dose titration. Methadone has a prolonged terminal half-life, so the degree of potential adverse effects can increase over several days after an initial dose or a change of dosage. The duration of methadone analgesia upon initiation may be only 6-8 hours. However, with repeated use, daily to three times daily dosing is effective.

Be cautious when converting from another opioid to methadone (Appendix C).^{95,96} As the MME/day rises, the methadone/morphine conversion ratio *declines* until methadone is approximately *twenty times* as potent as oral morphine (daily doses of morphine above 500 mg). Refer patients requiring high dose conversions to or from methadone to a specialist in pain management who has experience with methadone dosing.

During the first few days of methadone use, supplemental short-acting opioids may be used to manage inadequate analgesia, then discontinued. Educate the patient about the delayed response of both therapeutic and adverse effects for methadone. For this reason, avoid prescribing benzodiazepines or other sedatives along with methadone. For opioid-naïve patients, initiate methadone at very low doses (< 10 mg/day) divided into twice daily or three times daily dosing. For opioid-tolerant patients, initiate methadone using proper rotation ratios (Appendix C). Starting doses of methadone should not exceed 30 mg/day, even in opioid tolerant patients. Higher dose conversions may be indicated for some patients, but should prompt consultation with a pain management specialist. Regardless of starting dose, titrate (adjust) methadone doses in small increments (max 10-15% of total daily dose) not more often than once every 7 days. Typical methadone dosing for pain is in the range of 5-30 mg/day in divided doses. Higher doses enter the range of opioid addiction treatment.

Effect on QT interval. Methadone can prolong QT interval, especially at higher doses (≥ 100 mg/day) or when used in combination with other medications that prolong QT, including several classes of common antibiotics (eg, macrolides and quinolones). Perform periodic EKG monitoring for patients on higher doses of methadone, and for those being considered for methadone therapy if they are using other QT-prolonging medications (list available at www.qtdrugs.org).

Methadone testing. Methadone, like other opioid analgesics, is associated with a substantial risk for diversion. Mere confirmation of its presence on GC/MS, LC/MS or specific EIA testing (the "opioid" screening test misses methadone) may not be adequate. Prescribers should have a low threshold for periodic testing of serum levels. Specimens should be drawn knowing the variables of patient weight (kg), time since last dose taken (hours), and the total daily methadone dose (mg). Also, be aware of drug interactions that may affect an individual's methadone clearance. To estimate the expected serum trough level in ng/mL: $263 \times \text{total daily dose} \div \text{patient's weight}$. Methadone serum level peaks approximately two hours after dosing and fades over 5-6 hours. A peak level would be approximately double a trough level.

Buprenorphine. Buprenorphine is a partial agonist opioid that is potent and long-acting. Consider prescribing it when a safer, lower adverse effect profile is preferred over full agonist opioids, or for patients who have developed tolerance to other opioids.

Advantages of buprenorphine include its effectiveness, and lack of development of tolerance to it. As a

Schedule III drug, it may be written with refills for up to 6 months. Disadvantages include occasional problems with rash from transdermal patch use, and greater expense.

Transdermal buprenorphine (Butrans and generic) is FDA-approved for treating pain. It does not require an XDEA number or training to prescribe. The transdermal form is a good alternative for patients who have developed tolerance to other opioids, had a benefit from opioid treatment but wish to escalate treatment, and are taking ≤ 80 MME/day. Start with a 5 or 10 mcg patch (changed weekly), and discontinue other opioids.

Buccal buprenorphine (Belbuca) is also FDA-approved for pain treatment. It is given twice daily in patients who have previously been treated with opioid up to 160 MME/day. As with transdermal buprenorphine, it is effective, its misuse risk is low and its pharmacokinetics are not complicated. Cost can be a limiting factor.

Sublingual buprenorphine (Suboxone, Subutex and generic) may be prescribed off-label for pain with a regular DEA number. Sublingual buprenorphine has an evolving role, particularly in patients already treated with high dose opioid therapy who continue to complain of uncontrolled pain, and who may or may not have opioid use disorder. It offers a safer, effective option to full agonist opioids, has a lower risk for misuse, produces less opioid tolerance, causes fewer adverse effects, and can enhance mood. Unfortunately, its higher cost and lack of clinician knowledge of its proper use have so far limited its use as a pain treatment.

Initiation of sublingual buprenorphine can provoke acute opioid withdrawal if not done correctly. Therefore, only prescribers trained in its use and in possession of an XDEA number (or working under guidance of such a prescriber) should initiate sublingual buprenorphine/naloxone. Once a patient is on it and stable, primary prescribers may take over chronic management.

Fentanyl. Do not prescribe fentanyl for opioid naïve patients. Only consider prescribing fentanyl in a few unusual situations. Possible examples include: transdermal when gut mu receptors should be avoided; in head and neck cancer when oral intake is challenging; end of life care; intravenous in a patient with intrathecal "pain pump"; buccal and sublingual for episodic and breakthrough end-stage cancer pain.

Transdermal fentanyl (Duragesic and generic) has limited use for treatment of chronic pain. Transdermal fentanyl is a short-acting opioid packaged in a long-acting delivery system, making patients on it especially prone to development of opioid tolerance.

Transdermal fentanyl has a black box warning for opioid naïve patients. It should only be considered, even at low doses, for patients who are tolerant to opioids. Plasma levels of transdermal fentanyl are erratic and are influenced by several factors, including patient temperature, ambient humidity and temperature, skin thickness, presence of adipose tissue, and location of patch. The patch should never be placed on an open wound or mucous membrane. An expired transdermal patch still has a significant amount of fentanyl in it and must be discarded properly.

Dosing of transdermal fentanyl can be complicated; however, a general rule is that the dose of the patch in micrograms $\times 2$ is roughly equivalent to the oral MME/day. For example, a patient on a 50 mcg/hr patch (with a new patch every 3 days) is receiving approximately 100 MME/day ($50 \times 2 = 100$), and a patient on a 100 mcg/hr patch is receiving approximately 200 MME/day, etc. Transdermal fentanyl is commonly available in 12, 25, 50, 75, and 100 mcg/hr patches.

Buccal and lozenge fentanyl. Fentanyl "lollipops" (Actiq) are rapid-acting forms of fentanyl indicated for episodic and breakthrough end-stage cancer pain and generally, should not be prescribed. There is a black box warning on this formulation for using it only in opioid tolerant patients with a cancer-related diagnosis. Unfortunately, it has been used off label with alarming frequency in the last decade.

Fentanyl testing. Fentanyl is a synthetic opioid and its metabolites are often missed in urine drug screens.

GC/MS or LCMS are relatively good at detecting it and are reasonable confirmatory tests.

Adverse Effects of Opioid Analgesics

Recommendations:

In opioid naïve patients:

- Start opioids at low doses to avoid respiratory depression, which is most likely to occur in the first 24 hours. Use extra caution in patients with COPD or obstructive sleep apnea.
- Provide constipation prophylaxis.
- Consider anti-nausea medication.

When increasing opioid doses:

- Inform patients that temporary cognitive impairment may occur.
- If dosing increases to > 50 MME/day, prescribe naloxone to use if an overdose occurs.

With prolonged use of opioids, particularly with high doses:

- Consider that increased sensitivity to pain (opioid-induced hyperalgesia) may develop.
- Detoxification may be required.

Nearly 80% of patients using opioids experience adverse effects.⁹⁷ The most common adverse effects are sedation, nausea, headache, pruritus, and constipation. Other effects can be confusion, hallucinations, nightmares, urinary retention, dizziness, and headache. Tolerance and regression of most adverse effects often occur quickly. Constipation and urinary retention (smooth muscle inhibitory effects) are more persistent.

The most serious potential adverse effect is respiratory depression accompanied by symptoms of sedation and confusion. It may occur with high dose administration in opioid naïve patients. Opioids, at therapeutic doses, depress respiratory rate and tidal volume. As CO₂ rises, central chemoreceptors cause a compensatory increase in respiratory rate. Patients with impaired ventilatory reserve (COPD, asthma) are at greater risk of clinically significant respiratory depression. Tolerance to respiratory depression develops within just a few days.

In general, all opioids have similar adverse effects, including constipation, nausea, and rash, though constipation may be somewhat worse with oxycodone. For constipation, when initiating opioids, begin constipation prophylaxis using senna or polyethylene glycol 3350. Do **not** use docusate. During the first few days of treatment, consider anti-nausea medication. Nausea generally resolves after a few days and may be somewhat more common with codeine. Rash may be more common with morphine.

After an increase in dose, temporary cognitive impairment may occur. Tolerance to adverse cognitive effects usually develops quickly. Cognitive function, including the ability to drive, is preserved when on stable, moderate doses of opioids.

If opioid dosing is > 50 MME/day, prescribe naloxone. Higher opioid dosing increases the potential for overdosing.

With long-term use of opioids, an increased sensitivity to pain (called opioid-induced hyperalgesia) may develop, particularly when doses above those typically prescribed for pain are used. This may be one cause of apparent opioid tolerance, along with true pharmacologic tolerance and disease progression. Fortunately, tolerance to the analgesic effect, when it does occur, develops much more slowly than tolerance to these

adverse effects.

Detoxification will likely be required in patients with continued uncontrolled pain on high doses of opioids. Often detoxification can be accomplished by conversion to buprenorphine.

Patient's Informed Consent and Controlled Substance Agreement

Recommendations:

Use a Controlled Substance Agreement to assure that patients are informed of:

- The potential benefits, limitations, and specific risks of opioid treatment and alternative treatments.
- The conditions under which controlled substances will be prescribed, continued, tapered down, converted, or discontinued.

In Michigan, review the Start Talking Form and obtain the patient's signature verifying that state-mandated opioid education has been provided.

Before starting therapy, establish treatment goals. Focus on small measurable goals that emphasize function. Also discuss the discontinuation plan or "exit strategy" before prescribing. Educate the patient that if the above goals are not being met, then this would be a reason to discontinue opioid based therapy. This discussion is best done during an initial face-to-face visit and can be reiterated on follow up visits.

Prior to prescribing a controlled substance, review the Controlled Substance Agreement (CSA) with the patient. During the review, educate the patient about potential benefits, limitations, and significant risks of the treatment and alternative treatments. Patients must acknowledge that risks exist, that they accept taking those risks, and that they understand what is expected of them if treatment is to be continued. Standards of care for their safety include their submitting urine for toxicology testing and bringing their medication for counting. A CSA does not require a signature. Patients rarely object to a CSA. Any objection is a potential red flag for future problematic behavior. A sample CSA may be found in Appendix B.

In Michigan, laws regarding opioid prescribing require the patient to sign a Start Talking Form, in which they acknowledge in writing that they have been educated about the risks of opioid treatment. This is not the same as informed consent; the Start Talking Form does not meet the legal definition of consent. Instead, it is a document that verifies that education related to the harm of an opioid has been provided to the patient. However, reviewing risks, benefits, and alternatives is a good medical practice.

Advise patients to avoid alcohol while using an opioid. For patients who are pregnant or may become pregnant, discuss the risk of neonatal abstinence syndrome.

Safety Considerations

Recommendations:

Prescribe intranasal naloxone for patients at risk of overdose:

- History of overdose or substance use disorder
- Opioid dose > 50 MME/day
- Comorbidities, factors, or medications predisposing to sedation and suppressed breathing.

Educate patients, family, and friends about when and how to use intranasal naloxone and steps after administration.

Advise patients to store:

- Opioids in a secure location, preferably locked.
- Naloxone where it can be easily found and accessed.

Advise patients how to dispose of unused opioid medications safely and securely.

When to prescribe naloxone for opioid reversal. When opioid therapy is determined to be appropriate, consider prescribing intranasal naloxone as a safety strategy for opioid reversal. Consider naloxone for patients with:

- History of overdose
- History of substance use disorder
- Opioid dose > 50 MME/day
- Comorbidities or factors predisposing to sedation and suppressed breathing (eg, obstructive sleep apnea, significant pulmonary disease, cardiac disease, advanced age)
- Other drugs predisposing to sedation and suppressed breathing (eg, benzodiazepines).

Educate patients, family, and friends. When intranasal naloxone is prescribed, educate the patient and the patient's family and friends about when and how to use intranasal naloxone and steps after administration. Make sure they all know where naloxone is kept. For very vulnerable patients, consider a medical alert bracelet. Consider advising patients to label for others the location of naloxone in their home, such as a sign on the refrigerator or medicine cabinet.

Storage. Advise patients to store opioid medications in a secure location, preferably locked, that is away from household traffic. Opioids are a common reason for home invasion. Accidental ingestion by children and pets is also a concern.

Advise patients to store naloxone in a location where it can be easily found and accessed by the patient and others in an emergency. Store naloxone in a stable temperature environment in a highly visible and easy to access location. Most preparations of intranasal naloxone have a shelf life of 18 months. Instruct patients and families to check the expiration date frequently.

Disposal. Advise patients how to dispose of unused opioid medications safely and securely. Many options for disposal exist. Having unneeded opioids in the home is a vulnerability for patients and their families. Several disposal locations are available in pharmacies, law enforcement locations, hospital drop boxes, and at community take back events. Local pharmacies may sell over the counter tamper proof drug deactivation bags that can be placed in usual household trash.

Legal Considerations

Recommendations:

Prescribers must follow state and federal legal requirements when prescribing opioids and other controlled substances.

Do not prescribe opioids to treat opioid use disorder without the proper XDEA training.

Adhere to recommended guidelines and carefully document medical decision-making when prescribing opioids.

State and federal laws. Each prescriber must be aware of state and federal laws governing the prescription of opioids and other controlled substances. In Michigan, the law requires several actions by the prescriber when a controlled substance is prescribed.

Occasionally, clinicians may be asked, or are tempted to prescribe opioid analgesics as therapy for opioid use

disorder (illicit or prescription). This is *illegal*. Only prescribers with a XDEA may prescribe buprenorphine for the purpose of treating opioid use disorder. Methadone prescribed for opioid use disorder must be dispensed at a facility licensed by the DEA.

For clinicians interested in obtaining an XDEA number (waiver for buprenorphine prescribing) in the context of treating substance use disorder, contact the Michigan Opioid Collaborative (734-764-0231 or toll free 1-800-525-5188) or consult their website for information on waiver training.

Medicolegal risk. A 2017 review of malpractice claims involving the use of opioids for chronic pain found that a variety of patient and clinician factors contribute to poor outcomes and litigation. Medical comorbidities such as obstructive sleep apnea and cardiopulmonary disease, when combined with a long-acting opioid prescription, was identified as a particularly dangerous combination.⁹⁸ The authors advise that clinicians educate patients about the risks, benefits and alternatives of opioid therapy, perform adherence monitoring, and address aberrant behaviors. Careful documentation and adherence to guidelines are proposed to improve patient safety and minimize legal risk.

Opioids: Maintenance Phase

Monitoring Visits

Recommendations:

Frequency:

- After initiating an opioid, see the patient within 1-2 weeks. Then see them at least monthly until they reach a stable opioid dose with improvement in pain and function.
- When the opioid dose is stable, see the patient at regular intervals, but at least every 3 months.

Evaluation:

- Follow Checklist (Table 9).
- Check the state's prescription drug monitoring program report (called MAPS in Michigan).
- Obtain a urine drug screen at least once per year and any time when concerns arise for inappropriate use, the use of other substances, or diversion.
- Perform pill counts in high risk patients.

Medical Decision-Making:

- Reevaluate the risks and benefits of opioid analgesics for each patient.
- Do not exceed 50 MME/day unless clear evidence of benefit outweighs the risk. Avoid prescribing more than 90 MME/day.
- If a patient was previously stable on an opioid but requests an increase in dose, assess for tolerance or opioid failure. Consider if tapering down the opioid dose or converting to buprenorphine may be indicated.

An overview of prescribing for patients already taking opioids is presented in Figure 2.

Frequency. After initiating an opioid, see patients within 1-2 weeks, then at least monthly until the patient reaches a stable opioid dose with improvement in pain and function. This allows for close monitoring of opioid adverse effects, adherence and comorbidities.

When the opioid dose is stable with improvement in pain and function, see the patient at regular intervals, but

at least every 3 months (CDC guideline).¹¹

Evaluation at each follow up visit. Table 9 provides a checklist of items to accomplish at each visit. Obtain a history and exam to assess the effectiveness of the pain treatment plan as well as the risks and benefits associated with opioid analgesics. Assess pain characteristics, functional status, adverse effects, and adherence to the treatment plan. Review interval diagnostic testing and consults.

Particularly important is information about factors that increase the risk for adverse events or overdose, including decompensation of medical and psychiatric comorbidities, overdose potential, suicidality, as well as active use of other controlled substances, alcohol, marijuana, and illicit drugs.

To facilitate gathering information efficiently, use intake questionnaires or templates within the electronic health record. Consider how to involve clinical team members in the evaluation.

Check the state prescription drug monitoring program report (called MAPS in Michigan) each time a controlled substance is prescribed. Look for multiple prescribers, use of multiple pharmacies, unreported controlled substances, or other red flag behaviors (Table 10).

Urine drug testing. Obtain a urine drug screen (UDS) for all patients on chronic opioid therapy at least once per year, and any time there is a concern for inappropriate use, use of other substances, or diversion.⁹⁹

Urine drug testing is important for verifying the patient is actually using the prescribed medication, and is not selling it or providing it to others (called "diversion"). Urine drug testing also helps with patient safety, by assuring through testing that other sedating substances or medications are not in use. Interpreting test results requires knowledge and care because of the potential for false positive or negative results.¹⁰⁰ When in doubt, consult with your toxicology lab.

Conduct random testing at least yearly and more often if the patient is at additional risk for misuse or diversion for sale. The preferred testing strategy uses a combination of an enzyme linked immunoassay (EIA) for abused illicit substances and gas chromatography/mass spectroscopy (GC/MS) or liquid chromatography/mass spectroscopy (LC/MS). This approach provides the maximum specificity in detecting prescribed or illegally purchased medications that are typically missed by simple screening tests. At Michigan Medicine, order the "controlled medication management panel".

Three categories of results should raise concern:

- Presence of non-prescribed controlled substances
- Absence of prescribed medications (opioids or other medications)
- Presence of illicit drugs of abuse

Response to these results may include counseling, shortened follow-up intervals and urine testing, pill counts, referral for treatment of substance use disorder, or discontinuation of opioid therapy. See Appendix D for a guide to ordering and interpreting urine drug tests.

Reevaluate the risk/benefit of opioid analgesics. After reviewing the history, exam, and additional data, consider the risks and benefits of continuing opioid therapy. Perform this reevaluation at each visit.

Risk factors may develop during treatment that increase the potential harm of opioid treatment (ie, development of obstructive sleep apnea, new medication interactions, alcohol use, suicidal ideation). Opioids may no longer be resulting in a benefit for pain relief or improvement in functional capacity that warrants the opioid's risks.

If appropriate, modify opioid dosing. Always use the minimum effective opioid dose, or attempt to taper

down the dose. If an increased dose is to be tried, titrate the dose gradually, and do not exceed 50 MME/day unless clear evidence of benefit outweighs the risk. Avoid prescribing more than 90 MME/day (CDC guideline).¹¹ If an increased risk of harm or lack of effectiveness warrants a decrease in opioid dosing, begin a tapering down process. (See section on Discontinuing Opioids below.)

Requests for increases in medication. When patients request increases in opioid medication, perform a full reassessment of any new pain features and changes in psychosocial state. A request for additional opioids could indicate a new or worsened condition, increased tolerance, inappropriate opioid use, diversion, or opioid failure. Check the state prescription drug monitoring program report (called MAPS in Michigan). Perform urine drug testing. Consider doing pill counts. In most cases, avoid escalating opioid dosing for patients who were previously stable on an opioid regimen. A gradual tapering down of the opioid dose or a conversion to buprenorphine may be effective for these patients.

Managing the Prescription of Opioids

Recommendations:

Know state and federal regulations regarding controlled substance prescriptions.

Establish personal and office policies, roles, and processes that support and facilitate meeting prescribing requirements.

Understand regulations for prescribing controlled substances. Know state and federal regulations regarding controlled substance prescriptions. Key features include:

Schedule II controlled substance prescriptions shall be dated the date written, shall be for up to a one-month supply, cannot be phoned in, cannot have any authorized refills, and are valid for up to 60 days. A clinician may write a prescription dated today, but with instructions that the prescription not be filled for up to 60 days. In general, it is preferable to prescribe up to a 4-week supply (not 30 days), to avoiding marching into weekends. This requires becoming accustomed to writing 28, 56, or 84-count prescriptions.

Schedule III, IV, and V controlled substance prescriptions may be called in, with up to 6 months of refills.

All prescriptions shall be created and recorded in the medical record and should be readily retrievable. The information should include date prepared, the desired fill date, dose, quantity, and expected duration of use. E-prescribing is preferred and will soon be a requirement in many states, including Michigan.

Manage prescribing and refills. Establish personal and office policies, roles, and processes that support and facilitate meeting prescribing requirements. An example of policy for controlled substance prescription and refills is presented in Appendix G. The prescriber, patient, clinic staff, and covering prescribers should understand expectations and consequences. There should be no differences from in-person visits managing patients virtually. Video visits are preferred over phone visits and permit pill counts. Covering clinicians should NOT manage controlled substance prescriptions at night or on weekends.

Organize office procedures to meet prescribing requirements. See patients who are on a stable Schedule II-III opioid regimen every 2-3 months. Send in prescriptions to last until the next scheduled appointment or beyond to permit pill counts. For example, on one date, electronically send two 4-week prescriptions and specify a future fill date on one of the prescriptions. For patients taking a Schedule II opioid who are seen every 3 months, utilize clinic personnel to monitor prescription dispensing. Clinic staff can follow a protocol to ensure that the patient is up-to-date with appointments and appropriate monitoring. Staff can prepare a prescription for refill. After the clinician has reviewed appropriate information (including reviewing the state prescription drug monitoring program report), the clinician can electronically sign and send the prepared prescription. In general,

best practice is to give refills at face-to-face visits, thereby avoiding excess contacts to the office.

Patients on a stable dose of tramadol (Schedule IV) can be seen every 6 months. Refills for up to 6 months can be authorized on Schedule IV medication prescriptions. To avoid early refills, specify the fill dates for each refill in writing on the prescription.

Assess and Respond to Inappropriate Opioid Use

Recommendations:

Use established criteria to evaluate inappropriate opioid use by patients who are receiving long-term opioid therapy for chronic pain. Watch for red flag behaviors (Table 10).

Respond to suspicion of opioid misuse or diversion by collecting more information and discussing with the patient.

If criteria are met for the diagnosis of opioid use disorder:

- Initiate treatment for opioid use disorder, including use of medication assisted treatment (MAT).
- Continue to offer multimodal pain management therapies, emphasizing non-opioid strategies

Assess potential misuse of opioids. Use established criteria to evaluate misuse of opioids by chronic pain patients receiving long-term opioid therapy.¹⁰¹ Meeting 3 or more of the following criteria is defined as misuse.

1. **Focus on opioids.** The patient displays an overwhelming focus on opioids during visits. This focus occupies a significant proportion of the clinic visit time and impedes progress on other issues regarding the patient's pain. This behavior must persist beyond the third clinic treatment session.
2. **Early refills.** The patient demonstrates a pattern of requesting early refills (3 or more) or escalating drug use in the absence of an acute change in his or her medical condition.
3. **Multiple contacts about opioids.** The patient generates multiple telephone calls, visits, or other contacts to the administrative office requesting more opioids or early refills, or for problems associated with the opioid prescription.
4. **Prescription problems.** There is a pattern of prescription problems for a variety of reasons that may include lost, spilled, or stolen medications.
5. **Multiple sources of opioids.** The patient has supplemental sources of opioids obtained from multiple clinicians, emergency rooms, or illegal sources.
6. **Other substance misuse.** Concurrent illicit substance use or alcohol use disorder.

The authors of these criteria reported that 34% of chronic pain patients on opioids met at least one criterion, and 27% met 3 or more. These and other red flag behaviors are listed in Table 10.

Evaluating inappropriate opioid use. Respond to aberrant behaviors by collecting more information and discussing with the patient. Tools such as the drug abuse screening test ([DAST-10](#)) or Michigan opioid risk assessment (MORA) can be helpful in this effort. Check the state prescription drug monitoring program report. Perform a urine comprehensive drug screen to check for both the presence of non-prescribed medications or illicit substances and for the presence or *absence* of prescribed controlled substance medications. If opioid diversion is confirmed, discontinue the opioid prescription immediately. In most cases of opioid misuse, discontinuing opioid prescribing is indicated, using either a rapid or slow taper (see Discontinuing Opioids). Evaluate those patients who misuse opioid prescriptions for the presence of complex persistent dependence or opioid use disorder, and offer treatment.

Complex Persistent Dependence

Recommendations:

Consider the presence of complex persistent dependence in patients with high opioid doses (≥ 100 MME/day), impaired function, aberrant opioid use, psychiatric and substance use disorder comorbidities.

Do not escalate opioid doses for patients with complex persistent dependence.

Consider treatment with buprenorphine for patients with complex persistent dependence.

The gray area between dependence and addiction can be challenging for clinicians and patients. A 2012 article by Ballantyne, et.al. proposed a classification of complex persistent dependence that explains the pathophysiology accounting for worsening functional status and pain in patients on long-term opioid therapy.¹⁰²

When attempting to taper down opioid dosing for a patient with complex persistent dependence, aberrant behaviors and fluctuation in opioid use can occur. The development of protracted abstinence syndrome may lead to worsening pain, declining function, and worsening psychiatric symptoms. Paradoxically, the same symptoms may occur with maintenance of long-term high dose opioid therapy. Pain relief is more complex than analgesia measured by pain scales. Pain relief involves relief in the affective component of the pain experience, as mediated through mesolimbic reward and learning pathways involving the endogenous opioid system. This system is distinct from the pathways involved in nociceptive input. The same endogenous opioid pathways involved in reward are also involved in relief from other experiences including frustration, anger, anxiety, and despair. While analgesics like acetaminophen are thought to have effects on the analgesic pathways involved in nociception, opioids have additional effects on pathways that mediate relief. Opioids have a dual role in mediating direct relief on both analgesic pathways and reward pathways.

Some evidence shows that patients with complex persistent dependence may tolerate transition to buprenorphine better than a tapering down of the opioid dose. When complex persistent dependence is suspected, a more clinically useful approach may be to transition to buprenorphine and then taper down the dose. Start with careful communication with the patient about this strategy, including reassurances that the patient is not being treated "like an addict," and then refer to a buprenorphine waived prescriber.

Some evidence exists for methadone use in this population as well. However, it is less promising than buprenorphine.

Opioid Use Disorder in Pain Patients

Recommendations:

Use a standard tool such as the drug abuse screening test (DAST-10) to detect risk for medication misuse.

Monitor all patients on controlled substances by checking the state prescription drug monitoring program report with each prescription. Perform periodic urine drug testing. Pill counts are appropriate for the highest risk patients.

Prescribe naloxone to the highest risk patients.

Offer evidence-based treatment for addiction, including medication-assisted therapy

Substance use disorder complicating the treatment of chronic pain. The prevalence of substance use disorder among patients with chronic pain is significant. Studies have repeatedly demonstrated that at least 20% of opioid-treated patients misuse or divert their medication. In one survey 70% of patients reported *not*

taking their opioids as prescribed, often using them up quickly, then going without or obtaining opioids in illicit ways until due for their next refill.^{103,104}

Use drug misuse risk screening tools (such as the DAST-10) to help identify patients for whom risk might be managed by more frequent follow-up visits, checks of the state prescription drug monitoring program report, urine drug testing, or pill counts. However, these measures are imperfect. Risk screening tools can also aid in the decision that opioid risk exceeds the limited benefit for improving a patient's functional state.

A full discussion of the diagnosis and management of opioid use disorder is beyond the scope of this guideline. However, monitor patients for signs and symptoms of this disorder. Watch for red flag behaviors that may indicate addiction or diversion. Apply the DSM-5 diagnostic criteria to diagnose opioid use disorder, as listed below. (Mild opioid use disorder: 2-3 symptoms; moderate: 4-5 symptoms; severe: 6 or more symptoms):

- Opioids are often taken in larger amounts or over a longer period than intended.
- There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
- A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
- Craving, or a strong desire to use opioids.
- Recurrent opioid use resulting in failure to fulfill major role obligations at work, school, or home.
- Continued opioid use despite persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
- Important social, occupational, or recreational activities are given up or reduced because of opioid use.
- Recurrent opioid use in situations in which it is physically hazardous.
- Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.
- Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of opioids to achieve intoxication or desired effect, or (b) markedly diminished effect with continued use of the same amount of an opioid.

Principles for managing opioid use disorder in pain patients. The treatment of pain patients who exhibit evidence of opioid use disorder requires heightened monitoring, or discontinuation of opioid therapy and initiation of addiction treatment. Successful treatment depends on the clinician understanding that opioids provide more than analgesia, and that loss of control is not a moral failure by the patient, but a known complication of a reinforcing medication.

- Have a frank but supportive discussion with the patient about the fears of a worse lifestyle and risk for overdose. Offer support and addiction treatment.
- Provide support. A patient should not be made to feel judged, scorned, or abandoned by a clinician just because a diagnosis of opioid use disorder is made.
- Consider buprenorphine. For patients with opioid use disorder, conversion from other opioids to buprenorphine can provide a safer alternative while still providing the benefits, if any, of opioid analgesia. This can be done by a prescriber with a XDEA, with input from other specialists as needed.
- Refer when needed. If the complexity of a patient's management exceeds the capability of the prescriber, refer for formal addiction treatment.
- Do not continue to prescribe full agonist opioids for patients who exhibit loss of control over proper medication use or who use illicit substances. The risks for overdose or diversion outweigh any benefit.
- Prescribe naloxone and instruct the patient, family, and friends on its proper use.

When to Refer to a Pain or Addiction Specialist

Recommendations:

Refer chronic pain patients to appropriate specialists for multidisciplinary management of:

Clinical problems:

Outcome failure after 6 weeks of treatment

Ongoing adverse events

Unexpectedly large doses of opioids required

Frequent use of breakthrough dosing

Opioid-induced hyperalgesia

Opioid overdose

Need for conversion to sublingual buprenorphine

Behavioral problems:

Addiction or diversion suspicion

Non-adherence with Controlled Substance Agreement

When the management of patients with chronic pain involves difficult clinical or behavioral problems, refer the patient to an appropriate specialist or to multidisciplinary management.

Clinical problems for referral include:

- **Outcome failure.** Failure to attain adequate pain relief to achieve functional improvement goals after 6 weeks of opioid analgesic dose titration.
- **Adverse events.** Ongoing adverse effects of opioid therapy.
- **Unexpectedly large doses of opioids required.**
- Doses beyond what the primary care clinician is comfortable prescribing or beyond what are considered typically adequate for most pain management.
- Upper limits typically prompting referral are opioids in combination that exceed a total daily dose > 90 MME/day. (See Appendix C.) Also refer for individual medication doses greater than morphine 90 mg/day, hydrocodone 90 mg/day, oxycodone 60 mg/day, fentanyl 50 mcg/hr, hydromorphone 16 mg/day, methadone 30 mg/day.
- **Breakthrough dosing.** The patient requires additional dosing for breakthrough pain more than a few times per month.
- **Opioid-induced hyperalgesia.**
- **Opioid overdose**
- **Need for conversion to sublingual buprenorphine** if high opioid doses or insurance do not permit use of transdermal or buccal buprenorphine.

Behavioral problems for referral include:

- **Persistent behavior suspicious for addiction or diversion.**
- **Non-adherence with the Controlled Substance Agreement.**

Tapering Down and Discontinuing Opioids

Recommendations:

If opioid use is contraindicated, **discontinue prescribing immediately**, recognizing that withdrawal symptoms will likely occur. Example situations include illegal activity (eg, diversion, prescription forgery

or fraud), potential for immediate harm, or threatening behavior toward others.

If a patient is not following appropriate use instructions (eg, use of medication, monitoring visits, contract for refills), discontinue use with a **rapid taper** to minimize withdrawal symptoms.

If opioid has no benefit or produces clinical harms, discontinue with a **slow taper** to avoid withdrawal symptoms.

Explain the reasons for discontinuing the opioid medication. Explain the tapering down process.

If simple tapering down is not possible, consider referral to a specialist in addiction medicine.

Reasons for Discontinuing Opioids

Opioids may be discontinued for a variety of reasons, including diversion, prescription forgery or fraud, non-adherence to the treatment plan, lack of benefit, excessive dosing, a need to convert multiple opioids to a single opioid, or hospitalization. Opioid tapering and discontinuation can be challenging. Carefully consider each patient's medical, psychological, financial, and intellectual factors.

Speed of Discontinuation

The speed with which opioids are stopped depends on the situation. Options include immediate discontinuation, rapid taper, slow taper, buprenorphine conversion, and referral to an addiction specialist. See Appendix F for more information about these actions, along with associated reasons and recommended processes.

Immediate discontinuation. If controlled substance diversion, prescription forgery or fraud is discovered, immediately discontinue opioid prescribing. DEA regulations require that diversion for sale or prescription fraud be reported, so when these illegal activities are suspected, notify local law enforcement. Immediate discontinuation of opioids is also appropriate if there are dangerous behaviors with potential for immediate harm. Example situations include motor vehicle accident or arrest due to opioid or illicit drug or alcohol intoxication, intentional overdose, or suicide attempt. Aggressive or threatening behavior in the clinic can also be grounds for immediate discontinuation of opioids. When immediate discontinuation of opioid therapy is necessary, inpatient detoxification can be offered to help treat withdrawal.

Rapid taper. If a patient is not following appropriate use instructions, using a rapid taper to discontinue will prevent opioid withdrawal. The amount of opioid necessary to prevent withdrawal is only 20% of the previous day's dose (based on rapid detoxification studies). However, a rapid taper that reduces the dose by 25-50% per week over 2-4 weeks is commonly practiced.

Slow taper. If opioid treatment provides no benefit or produces clinical harm, discontinue with a slow taper to avoid withdrawal symptoms. The general rule for a slow taper is similar to initiation of therapy: use adjunct medications and non-pharmacological options (distraction, acupuncture, procedures, etc.) to help facilitate the tapering down process. Tapering down can be challenging, and patients may require frequent visits for reassurance or adjustments. Moreover, some opioid medications only are available in larger doses. Later in the tapering down process, converting to short-acting medications may be desirable to allow smaller dose changes over time. Generally, a slow taper that reduces the dose by 10% per week will prevent withdrawal, but it is important to know that the approach to tapering down must be individualized.

Explain Discontinuation

Prior to discontinuing an opioid, explain the tapering down process and the reasons for discontinuation. Some evidence shows that patients prefer to get this information from their primary care clinician or a clinician with whom they have a close relationship. Often, a patient's need for an intranasal naloxone rescue strategy can be

used to initiate and inform the conversation about why that patient may need to taper down the opioid dose. Providing a written taper schedule may be helpful. Scheduling regular check-in phone calls or telehealth visits can facilitate ongoing communication and increase adherence to a tapering down plan.

Complex Discontinuation

When a simple tapering down of the opioid dose is not feasible, consider referral to a specialist in addiction medicine. It is important to discuss the reason for this with the patient, addressing the social stigma of addiction and the rationale for referral.

Assuming Care for Patients Already on Opioids

Recommendations:

When assuming care for a patient already on opioids, perform a full assessment, confirming the diagnosis and need for opioids.

If continuing the use of opioids is appropriate, perform usual maintenance activities for monitoring, evaluation, and management.

If continuing the use of opioids is not appropriate, consider more appropriate treatments. Initiate tapering down and discontinuation of opioids.

When covering for a clinician in your practice, use procedures and precautions that apply to any follow-up visit by a patient on opioids.

When assuming care for a patient already on opioids, treat the patient like a new patient. Perform a full assessment of the patient's health and pain history. Document medications tried and failed and any prior response to opioids. This review is an opportunity for improvement in clinical care and for patient education.

If continuing the use opioids is deemed appropriate, perform all the usual activities for patients being maintained on opioids:

- **Prescription Drug Monitoring Program:** Check the state's prescription drug monitoring program website (called MAPS in Michigan) for controlled substance prescriptions. Look for multiple prescribers, use of multiple pharmacies, unreported controlled substances, and any other red flag behaviors (Table 10).
- **Urine drug screen:** Screen for both appropriate and inappropriate substances.
- **Start Talking Form (in Michigan):** Have the patient sign a new form before prescribing.
- **Controlled Substance Agreement:** Initiate a CSA before prescribing, if one is not already in place.

If continuing the use of opioids is not appropriate, as for any patient who no longer need be on opioids, consider more appropriate treatments. Initiate tapering down and discontinuation of opioids.

If you are covering for a clinician in your practice, the above procedures and precautions still apply, just as for any follow-up visit by a patient on opioids

For every patient on opioids, periodically review the risks, benefits, and alternatives to opioids (eg, use the Start Talking Form). Discuss any concerns about dose and duration, and review indications for intranasal naloxone.

Related National Guidelines and Performance Measures

National Guidelines

This guideline is generally consistent with the:

Institute for Clinical Systems Improvement (ISCI) guideline on Pain: Assessment, Non-Opioid Treatment approaches and Opioid Management. Best evidence for topics: recommendations and key references, pages 9 – 16.

Performance Measures

National and regional programs that have a clinical performance measure for care for the management of pain include the following.

- Centers for Medicare & Medicaid Services:
- Blue Cross Blue Shield of Michigan (BCBSM)
- Blue Care Network [HMO]: clinical performance measures (BCN)

While specific measurement details vary (eg, method of data collection, population inclusions and exclusions), the general measure is:

Documentation of Signed Opioid Treatment Agreement: All patients 18 and older prescribed opiates for longer duration than 6 weeks who signed an opioid treatment agreement at least once during Opioid Therapy documented in the medical record (CMS).

Guideline Development Methodology

Funding

The development of this guideline was funded by UMHS.

Guideline Development Team and Disclosures

The multidisciplinary guideline development team consisted of:

- Primary care clinicians: Daniel W. Berland, MD, General Internal Medicine/Addiction Medicine; Jill N. Fenske, MD, Family Medicine.
- Specialists in pain management care: SriKrishna Chandran, MD, Physical Medicine & Rehabilitation, Pain Medicine; Paul E. Hilliard, MD, Pain Medicine, Anesthesiology.
- Consultant specialists: Kimberly C. Bialik, PhD, Psychological Aspects of Pain Management; Daniel J. Clauw, MD, Anesthesiology, Internal Medicine-Rheumatology; Eve D. Losman, MD, Emergency Medicine; Kathleen S. Mehari, MD, Obstetrics & Gynecology; Michael A. Smith, PharmD, College of Pharmacy; and Susan Urba, MD, Hematology/Oncology.
- Guideline development methodologist: R. Van Harrison, PhD, Learning Health Sciences.
- Literature search services were provided by informationists at the Taubman Health Sciences Library, University of Michigan Medical School.

UMHS endorses the Standards of the Accreditation Council for Continuing Medical Education that the

individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Contributions of team members with relevant financial relationships are reviewed by team members without relevant financial relationships to assure the information is presented without bias.

None of the team members or consultants have relevant personal financial relationships.

Systematic Review of Literature

A detailed description of the systematic search and review of literature upon which this guideline is based is presented in the associated UMHS document "Ambulatory Pain Management, 2019: Literature Review Methods and Results." The following section highlights major aspects of the literature search and review process.

Literature search. The team began the search of literature by accepting the results of a systematic literature review performed in 2016:

Institute for Clinical Systems Improvement (ISCI) guideline on Pain: Assessment, Non-Opioid Treatment approaches and Opioid Management. Best evidence for topics: recommendations and key references, pages 9 – 16.

To update those results, we performed a systematic search of literature on Medline and in the Cochrane Database of Systematic Reviews for the time period 1/1/16—10/2/18.

The major search terms were acute and subacute pain, and chronic pain (non-terminal). The searches were for guidelines, controlled trials (including meta-analyses), and cohort studies, for literature on humans in the English language. Within these parameters individual searches were performed for the following topics:

Major Topic: Acute and Subacute Pain

- A. Acute and Subacute Pain: Etiologies of acute/subacute pain, Non-opioid therapies for acute/subacute pain, Use of opioids for acute/subacute pain, Universal precautions for opioid therapy, Acute and subacute pain, not included in A.

Major Topic: Chronic Pain (non-terminal)

- B. Chronic Pain Assessment: Pain characteristics (location, quality, intensity, time course), Pain treatment history, Determination of pain generator (focal pain generator, neuropathic pain, centralized pain syndrome), Quality of life and functional impact, Comorbidities (medical, psychiatric, substance use disorders), Pain beliefs and response to pain, Social determinants (adverse childhood experiences, psychosocial stressors), Chronic pain assessment, not included in B.
- C. Designing an Individualized Pain Treatment Plan: Multimodal interventions, Clinician-patient communication (shared decision-making, team approach), Individualized plan, not included in C.
- D. Non-Pharmacologic Treatments/evidence: Lifestyle management (exercise, sleep hygiene), Physical therapy, Other physical modalities (TENS, massage), Complementary and alternative therapies, Psychological interventions (mindfulness, CBT, etc.), Non-pharmacologic treatment, not included in D.
- E. Non-Opioid Pharmacologic Treatment: Acetaminophen, NSAIDs, Tricyclic, SNRI, Anticonvulsants, Muscle relaxants, Topicals not included in E, Non-opioid pharmacologic treatment, not included in E.
- F. Rational Use of Opioids in Chronic Pain; Decision Phase: Risk-benefit analysis (patient selection, risk analysis, informed consent), Assuming care for patients already on opioids, Special populations (pregnancy/lactation, geriatrics, renal disease, liver disease, pediatrics). (No search for "other")

- G. Rational Use of Opioids in Chronic Pain: Initiation and Treatment Phase: Drug selection and dosing (general guidance, CDC guidelines [most important example of general guidance]), Methadone, Fentanyl, Buprenorphine, Adverse effects, Controlled substance agreement, Safety considerations (avoid co-prescription with benzodiazepine, naloxone, storage, disposal), State of Michigan controlled substance legislation (no search), Opioids initiation/treatment, not included in G.
- H. Rational Use of Opioids in Chronic Pain: Maintenance Phase: Monitoring (frequency of visits, prescription drug monitoring programs, urine drug screening), Opioid refill management (office procedures), Assessing potential problems with opioid therapy, Response to suspicion for opioid misuse or diversion, Indications for referral to pain/addiction specialist, Legal issues, Medical marijuana, Opioid maintenance, not included in H.
- I. Tapering/Discontinuation of Opioids: Best practice for communication with patients about tapering, General tapering guidelines, Complex persistent dependence, Persistent abstinence syndrome, Opioid tapering/discontinuation, not included in I.
- J. Opioid Use Disorder: Detection, diagnosis, treatment (medication-assisted therapy), referral options, Chronic pain and opioids, not in J, Chronic pain, not included in J.

A more formal presentation of the inclusion and exclusion criteria is in Section II of the accompanying Literature Review Methods and Results.

The detailed search strategies are presented in Section III of the accompanying Literature Review Methods and Results.

The search was conducted in components of a formal problem structure (outlined above). The search was supplemented with very recent clinical trials known to expert members of the panel. The search was a single cycle. The number of publications identified is presented in Section IV of the accompanying Literature Review Methods and Results.

Literature review and assessment. Members of the guideline team reviewed the publications identified to be relevant to specific topics in order to select those with best evidence. Criteria to identify overall best evidence included relevance of the study setting and population, study design, sample size, measurement methods (variables, measures, data collection), intervention methods (appropriateness, execution), appropriateness of analyses, and clarity of description.

In considering level of evidence based on study design, the classification was:

A = systematic reviews of randomized controlled trials with or without meta-analysis

B = randomized controlled trials

C = systematic reviews of non-randomized controlled trials or observational studies, non-randomized controlled trials, group observation studies (cohort, cross-sectional, case-control)

D = individual observation studies (case study or case series)

E = expert opinion regarding benefits and harm.

Beginning with best evidence identified by the ISCI systematic literature review, team members checked publications identified in the more recent search (1/1/16—10/2/18) to determine whether better evidence was available. Team members also had the option of considering very recent literature (published since 10/2/18) in determining whether even better evidence was available.

The process of review and assessment is described in more detail in Section V of the accompanying Literature

Review Methods and Results.

Best evidence and recommendations. Team members identified articles or other publications with best evidence regarding specific topics.

The guideline team reviewed the evidence and determined the importance of performing or not performing key aspects of care (listed on the first page of this guideline). In the absence of empirical evidence, the guideline team based recommendations on their expert opinion.

The strength of recommendations regarding care were categorized as:

I = Generally should be performed

II = May be reasonable to perform

III = Generally should not be performed.

Section VI of the accompanying Literature Review Methods and Results presents a table of each recommendation and the source of best evidence on which the recommendation is based.

Review and Endorsement

A draft of this guideline was reviewed by units within UMHS to which the content is most relevant. Pharmacy Services performed the initial review. Then reviews occurred in clinical conferences or by distribution for comment within the following clinical departments and divisions: General Internal Medicine, Family Medicine, Physical Medicine & Rehabilitation, Pain Medicine, Anesthesiology, Clinical Psychology, Emergency Medicine, Obstetrics & Gynecology, Hematology/Oncology, and the Controlled Substances Quality Improvement Committee. The draft was revised based on comments from these groups.

The final version of this guideline was endorsed by the Clinical Practice Committee of the University of Michigan Medical Group and by the Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers.

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2009: Daniel W. Berland, MD; Philip E. Rodgers, MD; Carmen R. Green, MD; R. Van Harrison, PhD; Randy S. Roth, PhD. Consultants: Daniel J. Clauw, MD; Jennifer A. Meddings, MD; Ronald A. Wasserman, MD.

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Appendices

Appendix A1. Body Map

Appendix A2. PEG Scale Assessing Pain Intensity and Interference

Appendix A3. Chronic Pain Assessment Questionnaire

Appendix A4. Outline for Follow-up Visits for Patients with Chronic Pain

Appendix A5. DAST-10

Appendix A6. MORA

Appendix B. Patient-Clinician Agreement

Appendix C. Oral Opioid Dose Equivalents and Conversions

Appendix D. Ordering and Interpreting Urine Drug Tests

Appendix E. Summary of Michigan Legislation Related to

Appendix F. Discontinuing Opioids

Appendix G. Example Clinical Policy

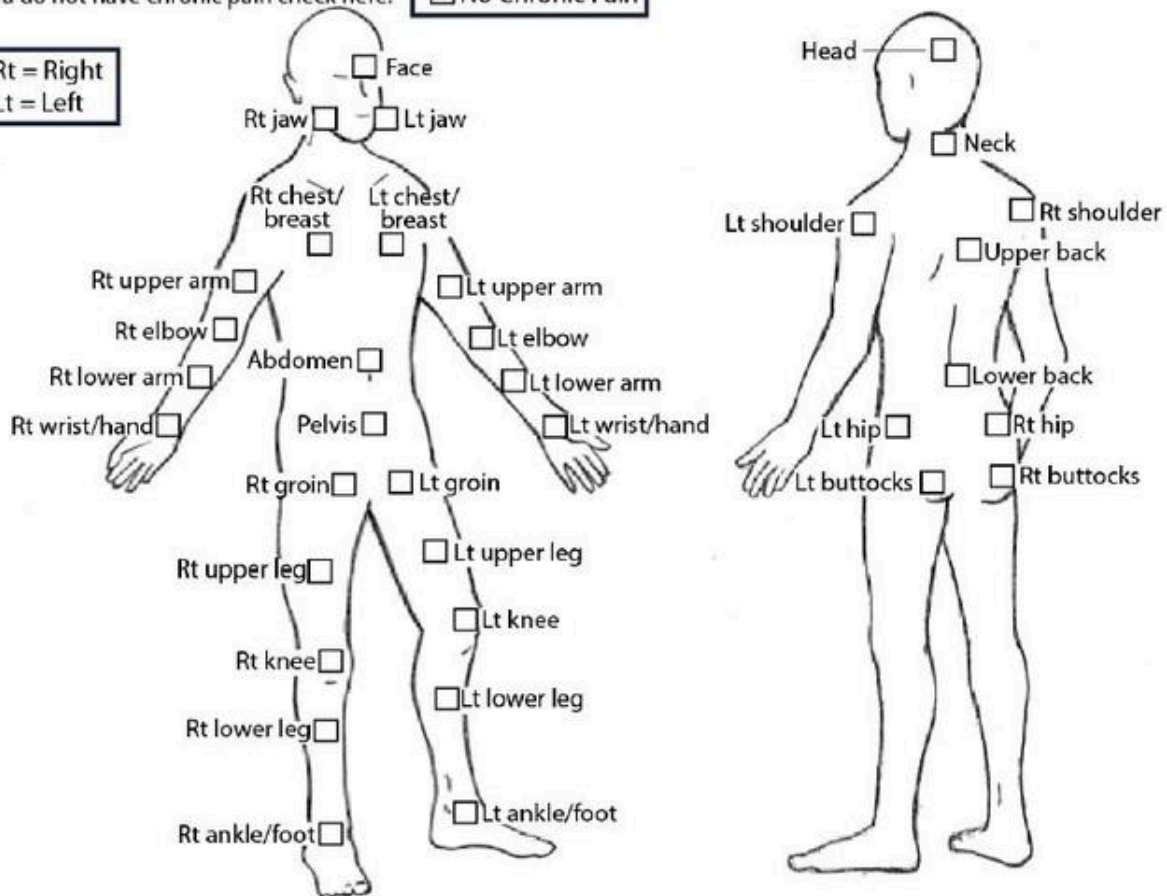
Appendix H. Resources and Websites

Appendix A1. Body Map

3 months or longer (chronic pain).

If you do not have chronic pain check here: ☐ No Chronic Pain

Rt = Right
Lt = Left



Appendix A2. PEG Scale Assessing Pain Intensity and Interference

(Pain, Enjoyment, General Activity)

1. What number best describes your pain on average in the past week?

0	1	2	3	4	5	6	7	8	9	10
No Pain			Pain as bad as you can imagine							

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere			Completely interferes							

3. What number best describes how, during the past week, pain has interfered with your general activity?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere			Completely interferes							

Computing the PEG Score.

Add the responses to the three questions, then divide by three to get a mean score (out of 10) on overall impact of points.

Using the PEG Score.

The score is best used to track an individual's changes over time. The initiation of therapy should result in the individual's score decreasing over time.

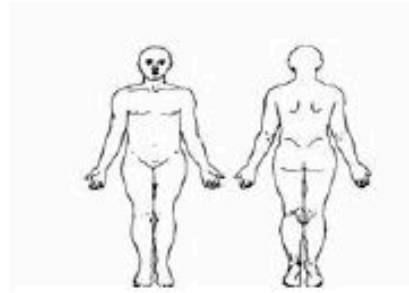
Source.

Krebs, E. E., Lorenz, K. A., Bair, M. J., Damush, T. M., Wu, J., Sutherland, J. M., Asch S, Kroenke, K. (2009). Development and Initial Validation of the PEG, a Three-item Scale Assessing Pain Intensity and Interference. *Journal of General Internal Medicine*, 24(6), 733–738. <http://doi.org/10.1007/s11606-009-0981-1>

Appendix A3. Chronic Pain Assessment Questionnaire

Date: _____

1. Where do you feel pain?
(shade areas on diagram to the right, put an x where it is worst)



2. Please rate your pain 1) at its worst intensity and 2) at its least intensity (please circle on the scale below) and then 3) place an "X" where your pain is right now.
(Low) 1 2 3 4 5 6 7 8 9 10 (High)

3. How much has pain interfered with your:

Normal Work	<input type="checkbox"/> None	<input type="checkbox"/> Some	<input type="checkbox"/> A lot	<input type="checkbox"/> Completely
Home Responsibility	<input type="checkbox"/> None	<input type="checkbox"/> Some	<input type="checkbox"/> A lot	<input type="checkbox"/> Completely
Hobbies/Recreation	<input type="checkbox"/> None	<input type="checkbox"/> Some	<input type="checkbox"/> A lot	<input type="checkbox"/> Completely
Social Activity	<input type="checkbox"/> None	<input type="checkbox"/> Some	<input type="checkbox"/> A lot	<input type="checkbox"/> Completely
Sleep	<input type="checkbox"/> None	<input type="checkbox"/> Some	<input type="checkbox"/> A lot	<input type="checkbox"/> Completely
Mood	<input type="checkbox"/> None	<input type="checkbox"/> Some	<input type="checkbox"/> A lot	<input type="checkbox"/> Completely

4. What are your goals for pain management? What do you need, or want to do but cannot because of your pain?

5. What new treatments (including medications) have you tried since your last visit?

6. How much have treatments (including medications) helped you do what you want, or what you need to do?

☐ None ☐ Some ☐ A lot ☐ Completely

7. Do you feel you need to take more pain medication than your doctor has prescribed?

☐ Yes ☐ No

8. Are you having any side effects or constipation from your medication?

☐ Yes ☐ No

9. What exercise have you performed recently? How many times per week? How long each time?

Type of Exercise	Times per week	How long each time?

Signature _____

Date _____

Page 1 of 1

POD-0300-01	REV: 7/09 HIM: 7/09	Image to CareWeb	 Michigan Medicine Hospitals and Health Centers	Pain Management Questionnaire
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Appendix A4. Outline for Follow-up Visits for Patients with Chronic Pain

Subjective	• Current pain history (quality, severity, provoking or palliating factors, radiation, time)
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	<ul style="list-style-type: none"> • Progress toward patient's goals (improvement of pain and functional status at work, home, recreation) • Adherence to multi-modal management plan, and barriers to adherence • Medications (adherence, frequency of use, adverse effects, interactions) • Status of medical or psychiatric comorbidities • Substance use (alcohol, tobacco, marijuana, illicit) • Social history (change in psychosocial determinants) • Red flag behaviors that may indicate addiction or diversion (Table 10) <p>Consider use of standardized instruments (MORA, DAST-10)</p>	
Objective	<ul style="list-style-type: none"> • Physical exam • Review updated imaging, diagnostic studies, reports from consultants • Urine drug screening (presence of and adherence to prescribed medication, absence of illicit and non-prescribed medication) • Check the state prescription drug monitoring program report (called MAPS in Michigan) for controlled substance prescriptions. Watch for multiple prescribers, use of multiple pharmacies, unreported controlled substance prescriptions, and any other red flag behaviors (Table 10). 	
Assessment	<ul style="list-style-type: none"> • Pain Generators • Functional Status • Response to Treatment • Comorbidities • Psychosocial Factors • Goals of care • Barriers and Resources • Risks and Benefits of Therapy 	
Plan	<ul style="list-style-type: none"> • Revise Individualized Pain Treatment Plan as needed: • Titrate (adjust) the dose of effective medications, and stop ineffective medications • Consider new modalities • Taper down and discontinue opioid dosing when there is no improvement in function, excessive dosing, risk for harm, or opioid use disorder. Consider buprenorphine. • Communication and education (build relationship, utilize clinical team members) • Consider referral to appropriate specialists if evidence of Opioid Use Disorder, failure to reach functional goals despite adherence to plan, rapidly escalating or very high dose opioid need, active psychiatric comorbidities, negative affect or pain beliefs. 	

Appendix A5. DAST-10

Drug Abuse Screening Test, DAST-10

The following questions concern information about your possible involvement with drugs *not including alcoholic beverages* during the past 12 months.

"Drug abuse" refers to (1) the use of prescribed or over-the-counter drugs in excess of the directions, and (2) any nonmedical use of drugs.

The various classes of drugs may include cannabis (marijuana, hashish), solvents (e.g., paint thinner), tranquilizers (e.g., Valium), barbiturates, cocaine, stimulants (e.g., speed), hallucinogens (e.g., LSD) or narcotics (e.g., heroin). Remember that the questions *do not* include alcoholic beverages.

Please answer every question. If you have difficulty with a statement, then choose the response that is mostly right.

In the past 12 months...		Circle	
1.	Have you used drugs other than those required for medical reasons?	Yes	No
2.	Do you abuse more than one drug at a time?	Yes	No
3.	Are you unable to stop abusing drugs when you want to?	Yes	No
4.	Have you ever had blackouts or flashbacks as a result of drug use?	Yes	No
5.	Do you ever feel bad or guilty about your drug use?	Yes	No
6.	Does your spouse (or parents) ever complain about your involvement with drugs?	Yes	No
7.	Have you neglected your family because of your use of drugs?	Yes	No
8.	Have you engaged in illegal activities in order to obtain drugs?	Yes	No
9.	Have you ever experienced withdrawal symptoms (felt sick) when you stopped taking drugs?	Yes	No
10.	Have you had medical problems as a result of your drug use (e.g. memory loss, hepatitis, convulsions, bleeding)?	Yes	No
Scoring: Score 1 point for each question answered "Yes," except for question 3 for which a "No" receives 1 point.		Score:	

Interpretation of Score		
Score	Degree of Problems Related to Drug Abuse	Suggested Action
0	No problems reported	None at this time
1-2	Low level	Monitor, re-assess at a later date
3-5	Moderate level	Further investigation
6-8	Substantial level	Intensive assessment
9-10	Severe level	Intensive assessment

Drug Abuse Screening Test (DAST-10). (Copyright 1982 by the Addiction Research Foundation.)

Appendix A6. MORA

Michigan Opioid Risk Assessment (MORA)

**THE PATIENT IS HIGH RISK FOR AN ADVERSE OPIOID EVENT
IF ONE OR MORE OF THE FOLLOWING IS PRESENT:**

MEDICAL CONSIDERATIONS	PSYCHIATRIC CONSIDERATIONS	SUBSTANCE USE CONSIDERATIONS
<ul style="list-style-type: none"><input type="checkbox"/> Age \geq 65 years<input type="checkbox"/> Dementia<input type="checkbox"/> Chronic respiratory failure requiring O₂<input type="checkbox"/> Sleep apnea<input type="checkbox"/> Cirrhosis<input type="checkbox"/> GFR < 30<input type="checkbox"/> Morphine milligram equivalence \geq 50 mg/day<input type="checkbox"/> History of opioid induced sedation or respiratory depression<input type="checkbox"/> Benzodiazepines<input type="checkbox"/> "Z" sleeping drugs (e.g., zolpidem, eszopiclone)<input type="checkbox"/> Muscle relaxants (carisoprodol, cyclobenzaprine, baclofen, tizanidine, etc.)<input type="checkbox"/> Barbiturates	<ul style="list-style-type: none"><input type="checkbox"/> Major psychiatric disorder<input type="checkbox"/> History of suicide attempt<input type="checkbox"/> Psychiatric symptoms possibly related to childhood emotional, physical or sexual trauma<input type="checkbox"/> Positive GAD-7 screen <i>see backside of page</i><input type="checkbox"/> Positive PHQ-9 screen <i>see backside of page</i><input type="checkbox"/> Positive PC-PTSD-5 screen <i>see backside of page</i>	<ul style="list-style-type: none"><input type="checkbox"/> Active substance use disorder (alcohol, non-medical use of pills, recreational drugs including cannabis)<input type="checkbox"/> History of substance use disorder<input type="checkbox"/> Medical marijuana use<input type="checkbox"/> Refusal to abstain from social alcohol use while on opioids<input type="checkbox"/> Unexpected PDMP report findings<input type="checkbox"/> Unexpected drug confirmatory test (presence of un-prescribed or illicit drug, or absence of prescribed drug)<input type="checkbox"/> Violation of a controlled substance agreement/ prior dismissal from controlled medication treatment<input type="checkbox"/> Aberrant "red flag" behaviors <i>see backside of page</i><input type="checkbox"/> Positive DAST-10 screen <i>see backside of page</i>

If an opioid is prescribed for pain, medical necessity along with a risk benefit assessment must be documented in the medical record.

Generalized Anxiety Disorder 7-item (GAD-7) scale

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all sure	Several days	Over half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it's hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3
Add score for each column	+	+	+	+
Total score = _____ (add your column scores)				
≥ 5 positive screen				

Patient Health Questionnaire (PHQ-9)

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all sure	Several days	Over half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too long	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or hurting yourself in some way	0	1	2	3
Add score for each column	+	+	+	+
Total score = _____ (add your column scores)				
≥ 5 positive screen				

PC-PTSD-5 scale

Sometimes things happen to people that are unusually or especially frightening, horrible, or traumatic. For example:

- a serious accident or fire
- a physical or sexual assault or abuse
- an earthquake or flood
- a war
- seeing someone be killed or seriously injured
- having a loved one die through homicide or suicide.

Have you ever experienced this kind of event?

☐ YES ☐ NO

If no, screen total = 0. Please stop here.

If yes, please answer the questions below.

In the past month, have you...

1. Had nightmares about the event(s) or thought about the event(s) when you did not want to?

☐ YES ☐ NO

2. Tried hard not to think about the event(s) or went out of your way to avoid situations that reminded you of the event(s)?

☐ YES ☐ NO

3. Been constantly on guard, watchful, or easily startled?

☐ YES ☐ NO

4. Felt numb or detached from people, activities, or your surroundings?

☐ YES ☐ NO

5. Felt guilty or unable to stop blaming yourself or others for the event(s) or any problems the event(s) may have caused?

☐ YES ☐ NO

≥ 3 positive screen

Drug Abuse Screening Test (DAST-10)

In the past 12 months...

1. Have you used drugs other than those required for medical reasons?

☐ YES ☐ NO

2. Do you abuse more than one drug at a time?

☐ YES ☐ NO

3. Are you unable to stop using drugs when you want to?

☐ YES ☐ NO

4. Have you ever had blackouts or flashbacks as a result of drug use?

☐ YES ☐ NO

5. Do you ever feel bad or guilty about your drug use?

☐ YES ☐ NO

6. Does your spouse (or parents) ever complain about your involvement with drugs?

☐ YES ☐ NO

7. Have you neglected your family because of your use of drugs?

☐ YES ☐ NO

8. Have you engaged in illegal activities in order to obtain drugs?

☐ YES ☐ NO

9. Have you ever experienced withdrawal symptoms (felt sick) when you stopped taking drugs?

☐ YES ☐ NO

10. Have you had medical problems as a result of your drug use (e.g. memory loss, hepatitis, convulsions, bleeding)?

☐ YES ☐ NO

≥ 1 positive screen

Red Flags for Prescribers

- Threatening/aggressive behavior towards staff or practitioner
- Sedated/intoxicated appearance
- Refusal to authorize release of medical records
- Refusal to sign controlled substance agreement
- Refusal to try non opioid therapies not previously prescribed
- Concurrent use of multiple pharmacies
- Recurrent ER pain visits for non-emergent pain
- Obtaining controlled substances from multiple prescribers
- Allergies or intolerances to multiple non opioid analgesics
- Fixating on controlled substances or requests for drugs by name
- Request for early controlled substance refills
- Lost or stolen controlled substance prescriptions
- Prescription tampering or forgery
- Misuse of controlled substances (obtaining from family/friends/streets)
- History or suspicion of controlled substance diversion
- Continuing to request and take opioids despite a lack of benefit and/or in the face of toxicity

Opioids can cause serious adverse events including sedation, respiratory depression, arrhythmias, addiction and death. There is also a risk for diversion. Universal precautions, biopsychosocial evaluation, risk assessment and informed consent are required before initiating or continuing opioid analgesics.

Appendix B. Patient-Clinician Agreement

Patient-Clinician Agreement for Ongoing Use of Controlled Medication	BIRTHDATE NAME
---	---------------------------

The use of the following medicine(s) _____

(list medicine names)

Is only one part of my treatment for _____.

Primary Prescribing Doctor: _____

What should I know about this medication?

This controlled medication may help me.

Opioid pain medications often have side effects, which may include but are not limited to:

- Itching
 - Rash
 - Severe constipation
 - Trouble urinating or passing stool
 - Depression getting worse
 - Problems thinking clearly
- Anxiety and sleep medicines can cause:

- Dizziness
 - Memory problems
- Combining drugs can cause:

- Overdose
- Trouble breathing
- Death

Stimulant medicines (such as for ADHD) can cause:

- High blood pressure
- Fast or irregular heart beats

I could become addicted to this medicine.

If I must stop this medicine for any reason, I need to stop it slowly. Stopping it slowly will help me avoid feeling sick from withdrawal symptoms. If I decide to stop my medication, I will contact my doctor.

If I or anyone in my family has ever had drug or alcohol problems, I have a higher chance of getting addicted to this medicine.

If I take this medicine and drink alcohol, use illegal drugs or use drugs prescribed by other clinicians:

- I may not be able to think clearly
- I could risk hurting myself (such as a car crash)
- I could become ill or even die

My doctor can only prescribe this medicine if I do not use illegal drugs.

If I do not use this medication exactly as prescribed, I risk hurting myself and others.

I will not increase my medicine dose without being told to do so by my doctor.

This medicine will not be refilled early.

I am in charge of my medicine.

- I know my medicine will not be replaced if it is stolen or lost.

- I will not share or give this medicine to other people.

BIRTHDATE

NAME

What can I do to help?

Bring my pill bottles with any pills that are left to each clinic visit.

When asked, I will give a urine and/or blood sample to help monitor my treatment. **I understand that clinic policy requires regular testing.**

Go to appointments and tests set up by my doctor. These may include physical therapy, x-rays, labs, mental health, etc.

If I miss my appointments, it may not be safe for me to stay on this medicine. If I miss appointments, my doctor may want an office visit before giving refills.

Be on time for appointments. If I arrive late to an appointment for prescription refills, my appointment may be re-scheduled. I may not be given my prescription until I am seen by my doctor.

Give my doctor permission to talk to my pharmacy. My doctor will check my prescription fill history by State Pharmacy registries and may call my pharmacy.

If my doctor decides that the risks outweigh the benefits of this medicine, my medicine will be stopped in a safe manner.

How can I get my prescriptions?

I can only get this prescription from my primary prescribing doctor's office.

I will not get controlled medications from other clinicians (including dentists, the Emergency Room, specialists or other clinicians), without checking with my primary prescribing doctor.

Controlled substance prescriptions are monitored. These prescriptions often need a paper-prescription signed by my doctor that cannot be mailed, faxed, or called to pharmacy. This type of prescription takes 24 hours before it will be ready for pick-up from clinic.

I will only use one pharmacy to fill these prescriptions.

Refills will be given **only** during normal office hours.

Clinic policy prevents on-call doctors from giving controlled substance prescriptions.

I know that unless my doctor tells me otherwise, I need a scheduled appointment to get prescription refills.

If my doctor decides it is safe for me to get a refill without an appointment, only I or someone I choose can pick up a prescription from the clinic. This person may be asked to show ID.

What are reasons for ending the agreement?

I may not be able to obtain controlled prescriptions from the University of Michigan Health System (UMHS) if I take more medication than is prescribed, if I fail to give requested urine or blood for testing, if those tests fail to contain the proper amounts of my prescribed medication, if non-prescribed medications (from friends, other prescribers, the ED, street purchases) are present, or if illegal drugs, including marijuana, are present.

I may not be able to be seen in this or any University of Michigan clinic if I am disruptive or threatening towards

staff.

I understand that under State of Michigan law, the non-medical use of controlled substances (lying to get medications, giving or selling these medicines to others) is a crime and will result in termination of controlled substance treatment by UMHS.

ATTESTATION:

Today, this treatment agreement has been reviewed with the patient and the implications explained. All questions were answered. After electronically signing, this agreement will be posted automatically to the medical record and a copy of this agreement will be printed and given to the patient for his/her own records.

Date _____

Appendix C. Oral Opioid Dose Equivalents and Conversions

Typical oral (every 4 hours) doses of short-acting opioids shown as equivalents to morphine:

Morphine	60 mg
Hydrocodone (Norco)	60 mg (equal to morphine potency)
Oxycodone	40 mg (1.5 x morphine potency)
Hydromorphone (Dilaudid)	12 mg (5 x morphine potency)
Oxymorphone (Opana) <i>Use of this is generally not recommended due to high expense and abuse rates.</i>	15 mg (4 x morphine potency)
Codeine (Tylenol #3 or #4)	360 mg (one-sixth morphine potency)

Dosing Principles

For patients requiring daily opioid therapy for longer than a few days to a few weeks, consider switching from short-acting opioids to long-acting oral therapy. Fentanyl patches are another option, but they are expensive, and it is difficult to titrate the dose. Conversion to methadone is also appropriate for patients requiring opioid use greater than several months, assuming opioids are effective for the patient. Buprenorphine is another option, particularly if opioid use disorder, opioid misuse, or extreme opioid tolerance is a risk.

First, convert any opioid in use to its equivalent amount of morphine in milligrams per day (MME/day). Then, divide into twice daily (or three times daily) Morphine ER doses. Methadone and fentanyl conversions are below.

Morphine to Methadone Conversion

Typical pain doses of methadone are 15-30 mg/day, given in 2-4 divided doses, whereas methadone doses used for treating addiction are higher and may reach 80-120 mg/day. Due to its function through NMDA receptors in addition to μ -receptors as well as its accumulation and excretion into the circulation from the liver, the relative potency of methadone to morphine increases *considerably* as morphine doses increase. Approximate equivalencies:

Oral Morphine Oral Methadone

30-90 mg	One fourth the morphine dose
90-300 mg	One eighth (200 mg/day morphine = 25 mg/day methadone)
300-500 mg	One twelfth the morphine dose
> 500 mg	One twentieth the morphine dose

Morphine to Fentanyl Patch Conversion

Each 2 mg of oral morphine per day is approximately equivalent to 1 mcg/hr fentanyl patch (eg, morphine 100 mg/day is approximately equivalent to a fentanyl 50 mcg/hr patch, applied every 3 days). Use caution in older adults and patients with cachexia; fentanyl is lipid soluble and requires subcutaneous fat for proper absorption.

Tapering Down the Opioid Dose

Slow taper. Reduce the opioid dose every 1-4 weeks by 10% of original dose until 20% remains. Then, taper down the remaining 20% by 5% of the original dose until the opioid has been discontinued, or the patient is at goal.

Rapid taper. Reduce the dose by 25% every 3–7 days, depending upon shorter vs. longer drug half-life.

Appendix D. Ordering and Interpreting Urine Drug Tests

When initiating or monitoring opioid therapy, two tests are often required. The two complimentary tests are the enzyme linked immunoassay (EIA) kit and gas or liquid chromatography/ mass spectrometry (GC/MS or LC/MS). They provide different information.

- Illicit drugs: EIA
- Confirm taking prescribed meds (specify meds when order test): GC/MS or LC/MS. (EIA will provide this information if your laboratory runs the test for each med. However, laboratories usually do not. *Ask!*)
- Use of non-prescribed medication: GC/MS or LC/MS
- Testing for heroin: GC/MS. Check for one of its specific metabolites, eg, 6 monoacetyl morphine (6-AM) duration 2-4 hours only is positive as morphine in 2-3 days

Enzyme linked immunoassay – EIA.

- Screening test for illicit substances amphetamine/ methamphetamine, marijuana, PCP, cocaine, "opiates" (eg, morphine/codeine)
- Inexpensive, fast, point of care or lab test
- Detects class of substance, not specific medication
- Will be negative for hydrocodone, hydromorphone, oxycodone, methadone, buprenorphine, benzodiazepines (particularly clonazepam) unless a specific test kit for those meds is in use. *Ask your lab!*
- High false positive rates caused by numerous prescribed or OTC meds

Gas or liquid chromatography/mass spectrometry – GC/MS or LC/MS. You must tell the laboratory the drugs you are seeking (patient is prescribed).

- More expensive, labor intensive
- Confirming test identifies specific meds and their metabolites. Use to confirm patient is taking prescribed meds and not taking non-prescribed meds
- High sensitivity
- False positives still occur

Interpretation of Results and Possible Causes

Results may be due to several possible causes.

- Illicit substance present: Use by patient; false result related to prescribed or OTC med exposure
- Non-prescribed medication present: Illicit use by patient; false positive testing – cross-reaction or possible known metabolite (hydrocodone can cause a false positive oxycodone test)
- Prescribed medication absent: diversion, or bingeing and running out early; false negative (incorrect use of EIA rather than GC/MS or LC/MS testing); urine adulterated

False positives. Are the results due to illicit use, a false positive on the screen, or a known metabolite of a prescribed medication? In considering prescribed medications, false positives on EIA (and GC/MS or LC/MS where specified) may result from:

- Amphetamines/methamphetamine: bupropion, tricyclic antidepressants, phenothiazines, propranolol, labetalol, OTC cold medications, ranitidine, trazodone. Vicks Nasal Spray can test positive even on GC/MS.
- Barbiturates: phenytoin
- Benzodiazepines: sertraline
- LSD: amitriptyline, doxepin, sertraline, fluoxetine, metoclopramide, haloperidol, risperidone, verapamil
- Opioids

- EIA testing: quinolones, dextromethorphan, diphenhydramine (Benadryl), verapamil, poppy seeds
- GC/MS testing

Morphine: from codeine, heroin (for a few hours), and poppy seeds for 48 hours

Hydromorphone: from morphine, codeine, hydrocodone, heroin

Oxycodone: from hydrocodone

Codeine: from hydrocodone

Fentanyl: from trazodone

Methadone: from quetiapine (Seroquel)

- PCP: dextromethorphan, diphenhydramine, NyQuil, tramadol, venlafaxine (Effexor), NSAIDs, imipramine
- Propoxyphene: methadone, cyclobenzaprine (Flexeril), doxylamine (NyQuil), diphenhydramine (Benadryl), imipramine
- Cannabinoids (on EIA not GC/MS): pantoprazole (Protonix), efavirenz (Sustiva, Atripla), NSAIDs

False negatives. Are the results due to the patient running out of medication early, diversion, a tampered specimen, or a threshold issue (eg, workplace testing using a high threshold for reporting a positive test to avoid false positives that require a job intervention)? For EIA (and GC/MS where specified) false negatives may result from:

- Unless bundled (*ask your lab!*), opioid immunoassays will miss fentanyl, meperidine, methadone, pentazocine (Talwin), oxycodone, tramadol, and often hydrocodone.
- Morphine: GC/MS may miss it unless glucuronide hydrolyzed. Can pick up with a specific test such as a specific qualitative EIA kit such as MSOPIATE. (*Ask your lab!*)
- Illnesses that cause lactic acidosis can cause false negatives
- Insensitivity of benzodiazepine screen: 40% or less sensitivity for alprazolam, lorazepam, clonazepam all frequently negative on both EIA and GC/MS.

Appendix E. Summary of Michigan Legislation Related to Controlled Substance Prescribing

Regulation	Pertinent Details
PA 0250 Requires health professionals to provide information on substance	Provide a list of substance use disorder services at the time of discharge from care.

use treatment services to patients who have experienced an opioid overdose.	
PA 0247 Requires prescribers to have a bona-fide clinician-patient relationship before prescribing controlled substances and specifies penalties for not meeting these requirements.	Ask and document other controlled substances being taken. Review the patient's records. Complete a full assessment of the patient's medical history and current medical condition, either in person or via telehealth. Provide follow-up care to monitor efficacy.
PA 0246 Requires prescribers to discuss and provide information about the dangers of opioids and obtain acknowledgement of that information prior to prescribing.	Excludes minors when treated for medical emergencies, surgery, hospice, oncology. Excludes all patients when prescribed for inpatient administration. Extensive content requirements. Requires patient/parent/guardian signature to be stored in the electronic record.
PA 0248 and PA 0249 Requires Michigan prescribers to register with MAPS and check MAPS when prescribing more than a three-day supply of a Schedule II - V controlled substance.	Ask and document other controlled substances being taken. Provide follow-up care to monitor efficacy. Excludes hospital/skilled nursing facility administrations.
PA 0251 Limits the supply of an opioid that could be prescribed for acute pain to a 7-day supply of an opioid within a 7-day period.	"Acute pain" is typically associated with invasive procedures, trauma, and disease, and usually lasts for a limited amount of time.
PA 0554 Amended the Public Health Code to provide for a voluntary nonopioid directive.	The nonopioid directive is a form that can be filled out by the patient (or a person's legal guardian or patient advocate) directing health professionals and emergency medical services personnel to not administer opioids to the patient. The form is available from the Department of Health and Human Services. Once submitted, the directive must be included in the patient's medical records. When a patient has this form on file, opioids should not be prescribed. There are exceptions in the law, such as a provision that a prescriber or a nurse under the order of a prescriber may administer an opioid if it is deemed medically necessary for treatment.

Appendix F. Discontinuing Opioids

Action	Reasons	Process
Discontinue Immediately	<ul style="list-style-type: none"> • Drug diversion, prescription forgery or fraud • Danger to the patient, eg, work, operation of machinery, suicide attempt • Threats are made in the practice office • Patient arrested 	No further prescribing.
Rapid Taper	<ul style="list-style-type: none"> • Non-compliance with evaluation or therapy plans (eg, tests, appointments, consultant visits) • Medication misuse • Problem ("red flag") behaviors (Table 10): focus on opioids, requests for early refills, multiple calls or visits, calls to Patient Relations, prescription problems, abnormal urine drug test results (positive or negative), illicit substance use, contract violations. 	<p>Multiple drug conversion. If multiple drugs, first convert all medications to MME/day (Appendix C) and taper down as morphine (using morphine sulfate extended release). If methadone is in use, convert to methadone equivalents.</p> <p>Rapid taper. Taper down by 25% every 3-7 days (shorter interval for short half-life medications). As little as 25% of the preceding dose may be used to avoid severe withdrawal.</p>
Slow Taper	<ul style="list-style-type: none"> • Lack of benefit (opioids are given on a trial basis) • Opioid-induced toxicity or hyperalgesia • Excessive dosing: morphine > 90 mg/day, oxycodone > 60 mg/day, fentanyl > 50 mcg/hour, methadone > 30 mg/day. 	<p>Multiple drug conversion. If multiple drugs, first convert all medications to MME/day (Appendix C) and taper down as morphine (using morphine sulfate extended release). If methadone in use, convert to methadone equivalents.</p> <p>Slow taper. Taper down by 10% of original dose every week until 20% remains. Taper down the remaining 20% by 5% of original dose each week until off or at goal.</p>
Buprenorphine Conversion with Tapering Down (requires XDEA number and experience)	<ul style="list-style-type: none"> • Opioids are not indicated and need to be stopped • Opioid-induced hyperalgesia is present due to high-dose opioid therapy requiring reduction • Pain and addiction are present 	<p>Referral for evaluation. Refer to chronic pain service for evaluation and clinic conversion.</p> <p>Evaluation during hospitalization. Evaluate patients with lack of benefit of opioids or with toxicity, who may benefit from conversion to buprenorphine.</p>

Appendix G. Example Clinical Policy

Clinic Policy Regarding Patients on Long-term Controlled Substances

(including opioids, benzodiazepines, and stimulants)

New Patients with a History of Long-term Use of a Controlled Substance

Before a new patient with a history of long-term controlled substance prescription use receives the first prescription from a clinic clinician, our clinic record must contain: the medical records, urine comprehensive drug test results, MAPS search results, and if long-term use is anticipated, a completed Controlled Substance Agreement.

Medical records. Patients must provide medical records documenting the medical workup related to the problem for which the controlled substance was prescribed, and notes from previous clinicians who prescribed these medications.

Obtain relevant medical records from previous clinicians. The patient is responsible for having this information sent. Our clinic staff can provide forms for release of information along with the fax number and mailing address of our clinic. The previous clinician's office should send the information directly to our clinic. Our clinic will also provide to the patient our clinic phone number so they can verify that the requested medical records have been received and can make appointments.

Use the suggested format outline for the initial clinic note. Include elements of the Past, Family, and Social histories that could put a patient at risk for medication problems. Include a detailed prescription history. Document the last time and date when the controlled substance was taken.

Urine comprehensive drug screen ("DRUG COMP"). DRUG COMP is combined immunoassay screening and gas chromatography/mass spectroscopy that together detect specific synthetic opioids along with morphine/codeine, benzodiazepines and drugs of abuse such as amphetamines, THC, and cocaine. It will also detect many common prescription meds such as tramadol, cyclobenzaprine, and tricyclic antidepressants (TCAs). (A SAMHSA Drug 5 or Drug 6 immunoassay screen is inadequate due to difficulty of interpretation and problems with false positives and negatives.)

Order a DRUG COMP screen for all new patients. To avoid false negatives, inform the lab in the test order if a specific opioid should be present. This is particularly important for methadone, fentanyl, and buprenorphine.

DRUG COMP specimen is collected in the clinic. Patients should not wear coats and other outer clothing nor take purses, bags, or backpacks into the bathroom. The nurse or clinician should confirm promptly that the specimen is appropriately warm and should send it directly to the lab, not give it to the patient to deliver.

Check for consistency between the drug screen results and the patient history. Check that no illicit drugs are present.

Michigan Automated Prescription System (MAPS). Search the state's online database of prescription fills controlled substances. Look for multiple prescribers or use of multiple pharmacies. Check for consistency between the report and the patient's history.

(MAPS: <https://michigan.pmpaware.net/login> for the patient's filling history. Clinicians should register at <https://milogintp.michigan.gov/uiseure/tpselfservice/anonymous/register> .)

Controlled Substance Agreement. If long-term use is anticipated, have the patient review and sign a Controlled Substance Agreement. Do this at the visit when the first controlled substance prescription is provided.

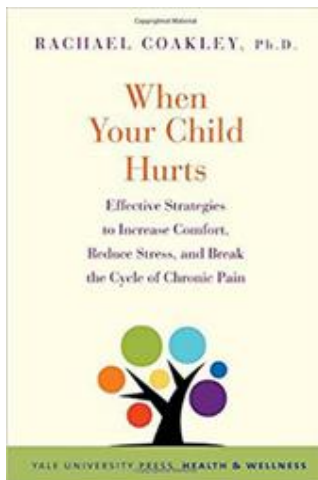
Appendix H. Resources and Websites

Information About Chronic Pain

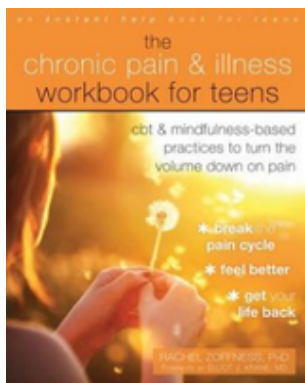


Managing Your Child's Chronic Pain, by Tonya Palermo is a good example of a book

that provides sound scientific knowledge and practical advice for parenting youth who have ongoing pain.



When Your Child Hurts, by Rachel Coakley provides families with basic information about what chronic pain is and how to deal with issues like, "How much do I push my child?", "Do I still make them go to school?" And other common issues faced by parents.



These books are not designed to replace good cognitive behavioral and family

therapy, but can be good additions to the work done in therapy.

The Chronic Pain and Illness Workbook for Teens, by Rachel Zoffness is designed specifically for teens who deal with chronic pain and fatiguing conditions. It takes the best of what we know about CBT and helps the teen apply it to their lives

Several websites designed to provide basic information about chronic pain and its treatment are listed below:

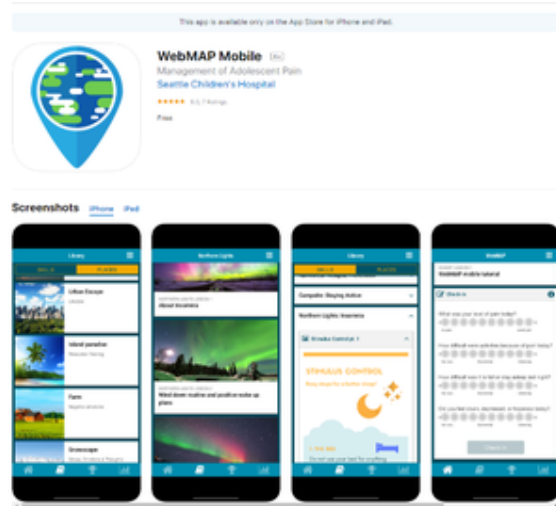
This online program is Cognitive Behavioral Therapy (CBT) based and can be done with or without a pain-

trained therapist.



PainBytes <http://www.aci.health.nsw.gov.au/chronic-pain/>

[painbytes](#)



A great option for treatment of Chronic Pain among adolescents is the WebMAP Mobile App. CBT and use of the techniques in the app have been shown to decrease pain, increase functioning and improve quality of life. Get it now in the App Store.

A good general website with resources for helping families cope with chronic pain is the www.MegFoundationforPain.org



A good general explanation of chronic pain: https://www.youtube.com/watch?v=C_3phB93rvI

A good resource for teachers is <http://teachpain.wordpress.com/pain-101/>

The TEACH-Pain Project

Search

Home Pain 101 What Teachers Need To Know What Teachers Can Do Frequently Asked Questions Resources

Finding a Local Counselor

<https://umcpd.umich.edu/>

ADAA - <https://members.adaa.org/page/FATMain>

CHRONIC PAIN COPING RESOURCES

Books: Pain is really strange by Stephen Haines

Websites:

[Neuroplasticity Transformation: Dr. Moskowitz and Dr. Golden](#)

[Curable App](#)

[American Chronic Pain Association](#)

[U of M Fibro Guide](#)

[Palouse Mindfulness](#)

<https://mobile.va.gov/appstore/mental-health> for various apps

The VA has a page specific to chronic pain https://www.va.gov/PAINMANAGEMENT/Veteran_Public/CHRONIC_PAIN_101.asp

APPROVALS

P&T	Date: 11/17/2020
Pain Committee	Date: 10/15/2020
CPC	Date: 12/4/2020
ECCA	Date: 1/12/2021

Literature search service

Taubman Health Sciences Library

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

Attachments

[Visit Checklist for Established Patients on Long-term Controlled Substances](#)

[Appendix B: Patient-Provider Agreement for Ongoing Use of Controlled Medication](#)

[Appendix A.3: Opioid Risk Tool](#)

Applicability

Michigan Medicine Public, UMHS Clinical